2018 ESC Pocket Guidelines

Committee for Practice Guidelines

Z.F

SYNCOPE

Guidelines for the Diagnosis and Management of Syncope

ESC
European Society of Cardiology

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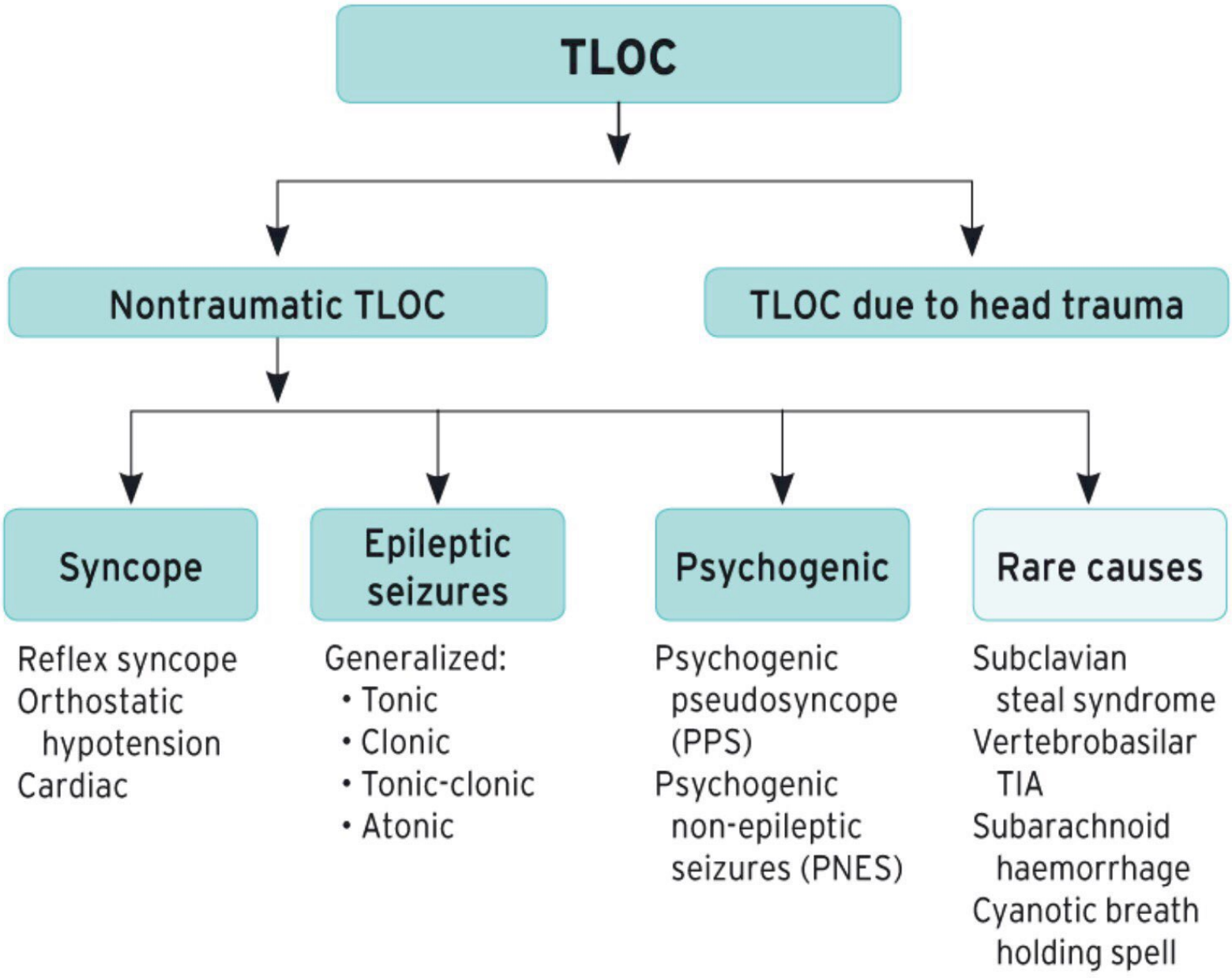
- Syncope is defined as transient loss of consciousness (TLOC) due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recovery.

Syncope shares many clinical features with other disorders: it therefore presents in many differential diagnoses. This group of disorders is labelled TLOC.

- TLOC is defined as a state of real or apparent LOC with loss of awareness, characterized by amnesia for the period of unconsciousness, abnormal motor control, loss of responsiveness, and a short duration.

Figure 1 Syncope in the context of TLOC



TIA = transient ischaemic attack; TLOC = transient loss of consciousness.

Table 1 Classification of syncope

Reflex (neurally mediated) syncope

Vasovagal:

- Orthostatic vasovagal syncope (VVS): standing, less common sitting
- Emotional: fear, pain (somatic or visceral), instrumentation, blood phobia

Situational:

- Micturition
- Gastrointestinal stimulation (swallow, defaecation)
- Cough, sneeze
- Post-exercise
- Others (e.g. laughing, brass instrument playing)

Carotid sinus syndrome

Non-classical forms (without prodromes and/or without apparent triggers and/or atypical presentation)

Syncope due to orthostatic hypotension (OH)

Drug-induced OH (most common cause of OH):

- e.g. vasodilators, diuretics, phenothiazine, antidepressants

Volume depletion:

- Haemorrhage, diarrhoea, vomiting, etc.

Primary autonomic failure (neurogenic OH):

- Pure autonomic failure, multiple system atrophy, Parkinson's disease, dementia with Lewy bodies

Secondary autonomic failure (neurogenic OH):

- Diabetes, amyloidosis, spinal cord injuries, auto-immune autonomic neuropathy, paraneoplastic autonomic neuropathy, kidney failure

Cardiac syncope

Arrhythmia as primary cause:

Bradycardia:

- Sinus node dysfunction (including bradycardia/tachycardia syndrome)
- Atrioventricular conduction system disease

Tachycardia:

- Supraventricular
- Ventricular

Structural cardiac: aortic stenosis, acute myocardial infarction/ischaemia, hypertrophic cardiomyopathy, cardiac masses (atrial myxoma, tumours, etc.), pericardial disease/tamponade, congenital anomalies of coronary arteries, prosthetic valve dysfunction

Cardiopulmonary and great vessels: pulmonary embolus, acute aortic dissection, pulmonary hypertension

- There are two main pathophysiological mechanisms in reflex syncope. “Vasodepression” refers to conditions in which insufficient sympathetic vasoconstriction results in hypotension. “Cardioinhibition” is used when bradycardia or asystole predominates, reflecting a shift towards parasympathetic predominance. The haemodynamic pattern, i.e. cardioinhibitory, vasodepressive, or both, is independent of the trigger evoking reflex syncope. For example, micturition syncope and orthostatic VVS may equally well present as cardioinhibitory or as vasodepressor syncope.
- The non-classical form of reflex syncope involves a heterogeneous group of patients. The term is used to describe reflex syncope that occurs with uncertain or apparently absent triggers and/or atypical presentation. The diagnosis of reflex syncope is probable when other causes of syncope are excluded (absence of structural heart disease) and/or symptoms are reproduced in the tilt test. At present, this group also contains syncope associated with low adenosine plasma levels.
- The cardiovascular causes of orthostatic intolerance include classical OH, initial OH, delayed OH, postural orthostatic tachycardia syndrome (POTS), and VVS, which in this context can be called orthostatic VVS.

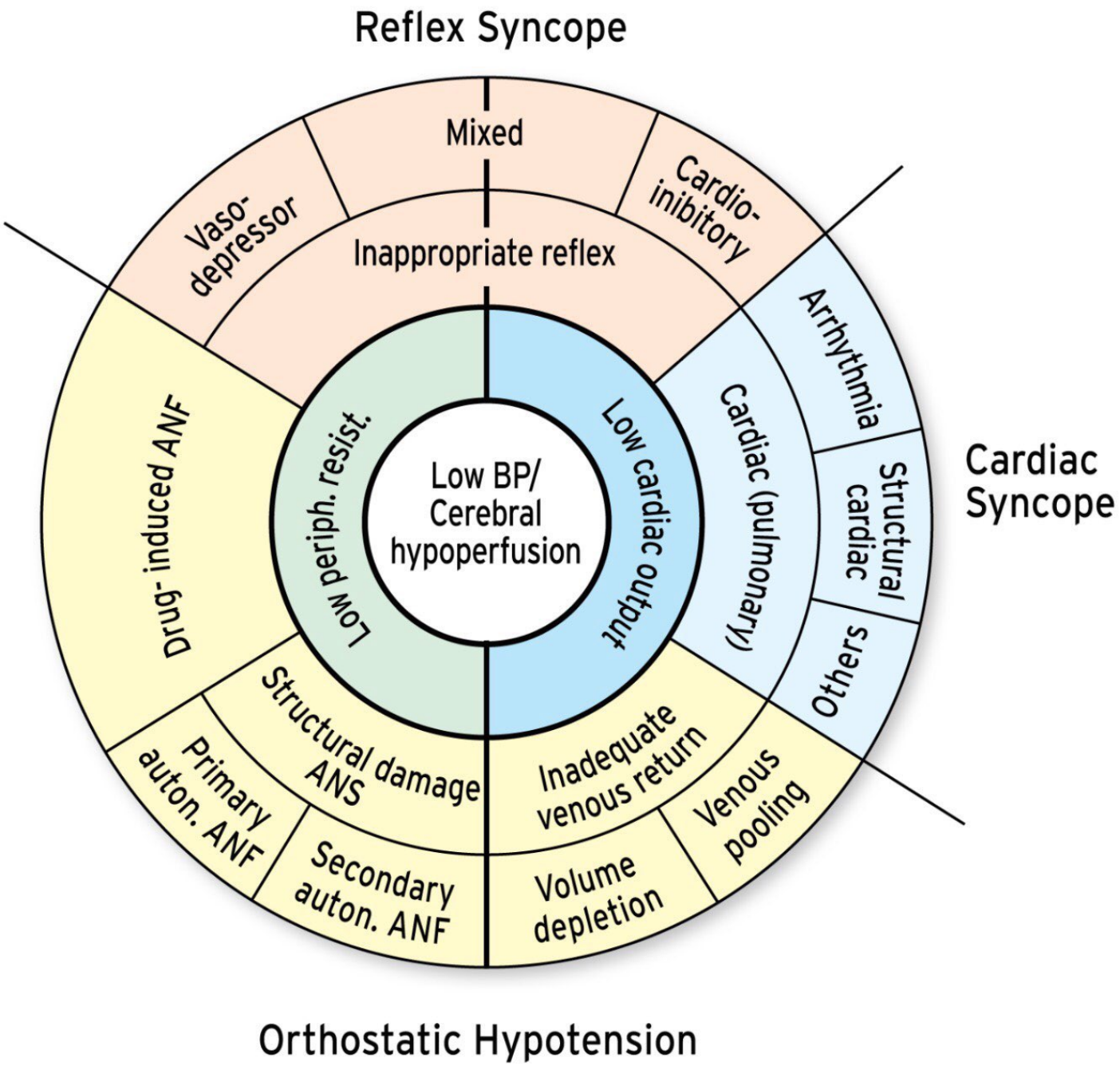
Table 2 Conditions which may be incorrectly diagnosed as syncope

Condition	Characteristic features that distinguish from syncope
Generalized seizures	See section (Neurological causes...). Table 6 (Differentiating syncope from epileptic seizures).
Complex partial seizures, absence epilepsy	No falls, yet unresponsive and later amnesia.
PPS or "pseudocoma"	Duration of apparent LOC lasting many minutes to hours; high frequency, up to several times a day.
Falls without TLOC	No unresponsiveness or amnesia.
Cataplexy	Falls with flaccid paralysis and non-responsive, yet no later amnesia.
Intracerebral or subarachnoid haemorrhage	Consciousness may be progressively reduced rather than immediately lost. Accompanying severe headache, other neurological signs.
Vertebrobasilar TIA	Always focal neurological signs and symptoms, usually without LOC; if consciousness is lost this usually lasts longer than in TLOC.
Carotid TIA	Consciousness is for all practical purposes not lost in carotid TIAs, but there are pronounced focal neurological signs and symptoms.
Subclavian steal syndrome	Associated with focal neurological signs.
Metabolic disorders including hypoglycaemia, hypoxia, hyperventilation with hypocapnia	Duration much longer than in TLOC; consciousness may be impaired instead of lost.
Intoxication	Duration much longer than in TLOC; consciousness may be impaired instead of lost.
Cardiac arrest	LOC yet no spontaneous recovery.
Coma	Duration much longer than TLOC.

LOC = loss of consciousness; PPS = psychogenic pseudosyncope; TIA = transient ischaemic attack; TLOC = transient loss of consciousness.

The pathophysiological classification centres on a fall in systemic blood pressure (BP) with a decrease in global cerebral blood flow as the defining characteristic of syncope. Figure 2 shows low BP and global cerebral hypoperfusion as the central final common pathway of syncope. A sudden cessation of cerebral blood flow for as short as 6-8 seconds can cause complete LOC. A systolic BP of 50–60 mmHg at heart level, i.e. 30–45 mmHg at brain level in the upright position, will cause LOC.

Figure 2 Pathophysiological basis of the classification of syncope



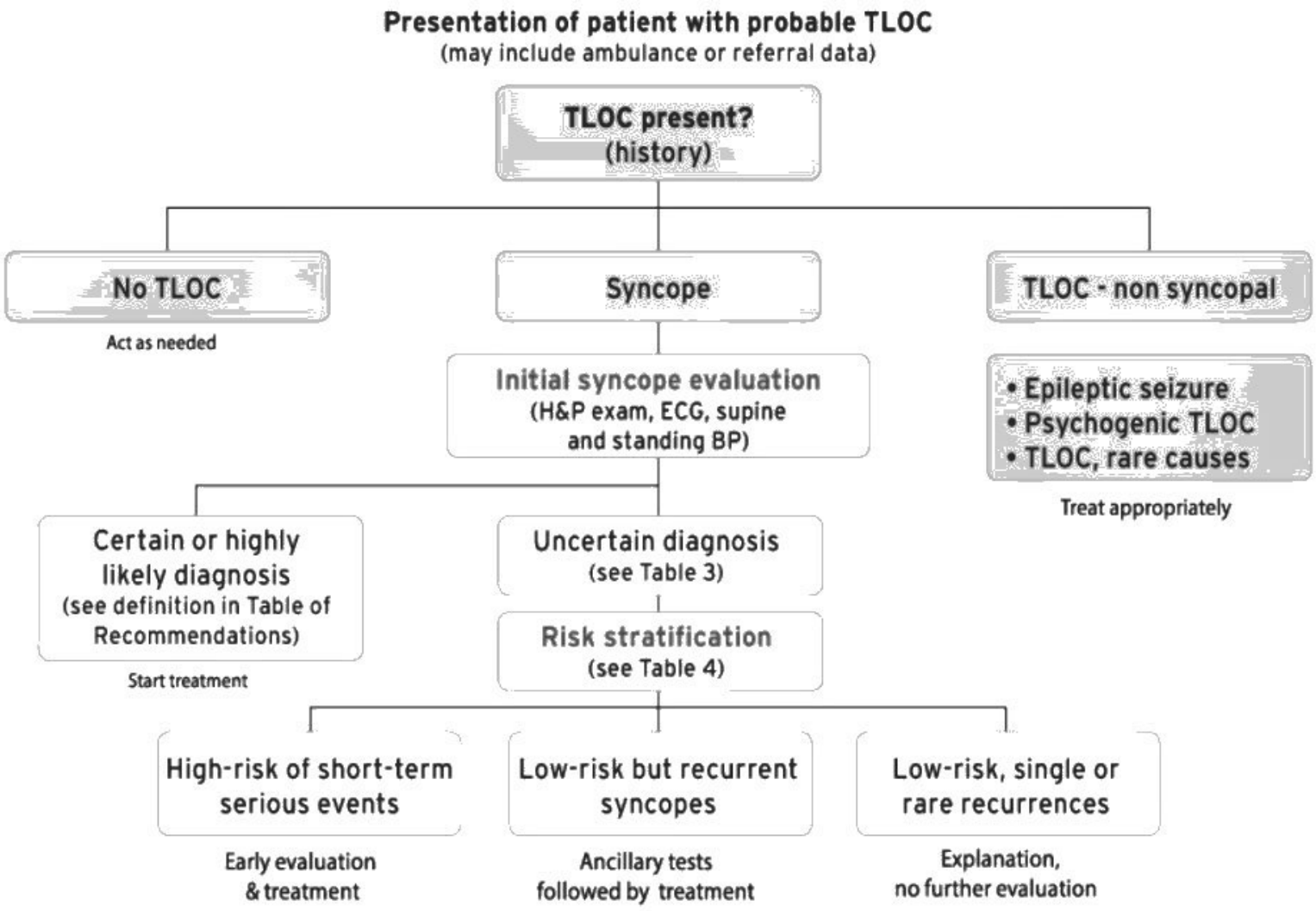
ANF = autonomic nervous failure; ANS = autonomic nervous system; auton. = autonomic; BP = blood pressure; OH = orthostatic hypotension; periph. = peripheral; resist. = resistance.

The initial evaluation should answer key questions:

1. Was the event TLOC?
2. In case of TLOC, is it of syncopal or non-syncopal origin?
3. In case of suspected syncope, is there a clear aetiological diagnosis?
4. Is there evidence to suggest a high risk of cardiovascular events or death?

TLOC is probably syncope when: a) there are signs and symptoms specific for reflex syncope, syncope due to OH, or cardiac syncope, and; b) signs and symptoms specific for other forms of TLOC (head trauma, epileptic seizures, psychogenic TLOC, rare causes) are absent.

Figure 3 Flow diagram for initial evaluation and risk stratification of patients with syncope



BP = blood pressure; ECG = electrocardiogram; H&P exam = history and physical examination; TLOC = transient loss of consciousness.

For interactivity see here

The initial syncope evaluation consists of:

- Careful history taking concerning present and previous attacks, as well as eyewitness accounts, in person or through a telephone interview;
- Physical examination, including supine and standing BP measurements; and
- Electrocardiogram (ECG).

Based on these findings, additional examinations may be performed when needed:

- Immediate ECG monitoring when there is a suspicion of arrhythmic syncope;
- Echocardiogram when there is previous known heart disease or data suggestive of structural heart disease or syncope secondary to cardiovascular cause;
- Carotid sinus massage (CSM) in patients age >40 years;
- Head-up tilt testing when there is suspicion of syncope due to OH or reflex syncope; and
- Blood tests when clinically indicated, e.g. haematocrit or haemoglobin when haemorrhage is suspected, oxygen saturation and blood gas analysis when hypoxia is suspected, troponin when cardiac-ischaemia related syncope is suspected, D-dimer when pulmonary embolism is suspected, etc.

Recommendations - Diagnostic criteria with initial evaluation		
Recommendations	**Class[a]**	**Level[b]**
Reflex syncope and OH		
1. VVS is highly probable if syncope is precipitated by pain, fear or standing, and is associated with typical progressive prodrome (pallor, sweating, nausea).	I	C
2. Situational reflex syncope is highly probable if syncope occurs during or immediately after specific triggers, listed in Table 1.	I	C
3. Syncope due to OH is confirmed when syncope occurs while standing and there is concomitant significant OH.	I	C
4. In the absence of the above criteria, reflex syncope and OH should be considered likely when the features that suggest reflex syncope or OH are present and the features that suggest cardiac syncope are absent (see Table 3).	IIa	C
Cardiac syncope		
5. Arrhythmic syncope is highly probable when the ECG shows: • Persistent sinus bradycardia <40 b.p.m. or sinus pauses >3 seconds in awake state and in absence of physical training • Mobitz II second- and third-degree AV block • Alternating left and right BBB • VT or rapid paroxysmal SVT • Non-sustained episodes of polymorphic VT and long or short QT interval • Pacemaker or ICD malfunction with cardiac pauses.	I	C
6. Cardiac-ischaemia– related syncope is confirmed when syncope presents with evidence of acute myocardial ischaemia with or without myocardial infarction.	I	C
7. Syncope due to structural cardiopulmonary disorders is highly probable when syncope presents in patients with prolapsing atrial myxoma, left atrial ball thrombus, severe aortic stenosis, pulmonary embolus, or acute aortic dissection.	I	C

AV = atrioventricular; BBB = bundle branch block; b.p.m. = beats per minute; ECG = electrocardiogram; ICD = implantable cardioverter defibrillator; OH = orthostatic hypotension; SCD = sudden cardiac death; SVT = supraventricular tachycardia; VT = ventricular tachycardia; VVS = vasovagal syncope.
[a]Class of recommendation - [b]Level of evidence.

When a diagnosis is nearly certain or highly likely, no further evaluation is needed, and treatment - if any - can be planned. In other cases, the initial evaluation may suggest a diagnosis when the features listed in Table 3 are present, or otherwise is unable to suggest any diagnosis.

Table 3 Clinical features that can suggest a diagnosis on initial evaluation

Reflex syncope

- Long history of recurrent syncope, in particular occurring before the age of 40 years
- After unpleasant sight, sound, smell, or pain
- Prolonged standing
- During meal
- Being in crowded and/or hot places
- Autonomic activation before syncope: pallor, sweating, and/or nausea/vomiting
- With head rotation or pressure on carotid sinus (as in tumours, shaving, tight collars)
- Absence of heart disease

Syncope due to OH

- While or after standing
- Prolonged standing
- Standing after exertion
- Post-prandial hypotension
- Temporal relationship with start or changes of dosage of vasodepressive drugs or diuretics leading to hypotension
- Presence of autonomic neuropathy or parkinsonism

Cardiac syncope

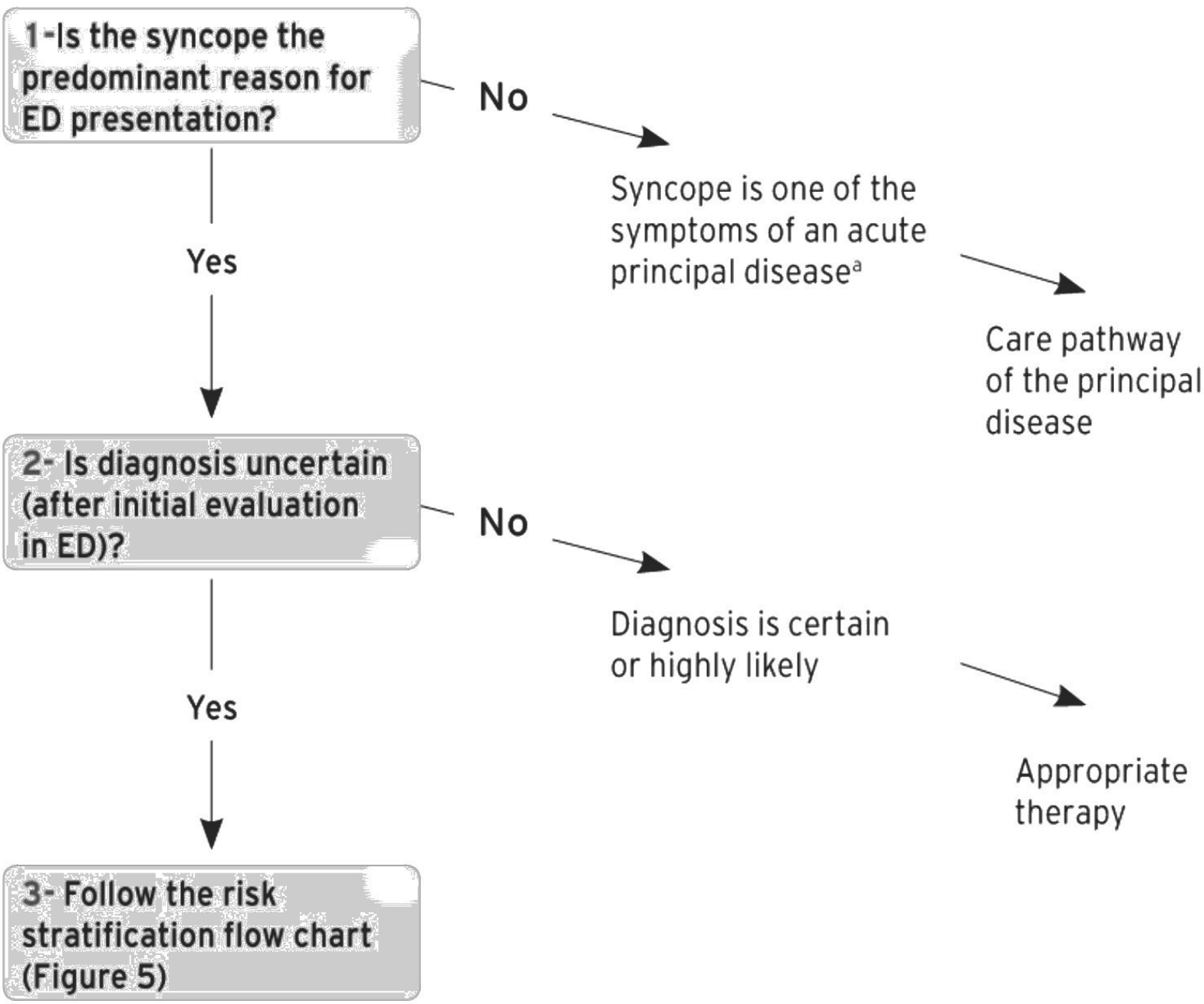
- During exertion or when supine
- Sudden onset palpitation immediately followed by syncope
- Family history of unexplained sudden death at young age
- Presence of structural heart disease or coronary artery disease
- ECG findings suggesting arrhythmic syncope:
  - Bifascicular block (defined as either left or right BBB combined with left anterior or left posterior fascicular block)
  - Other intraventricular conduction abnormalities (QRS duration ≥0.12 s)
  - Mobitz I second-degree AV block and first-degree AV block with markedly prolonged PR interval
  - Asymptomatic mild inappropriate sinus bradycardia (40–50 b.p.m.) or slow atrial fibrillation (40–50 b.p.m.) in the absence of negatively chronotropic medications
  - Non-sustained VT
  - Pre-excited QRS complexes
  - Long or short QT intervals
  - Early repolarization
  - ST-segment elevation with type 1 morphology in leads V1–V3 (Brugada pattern)
  - Negative T waves in right precordial leads, epsilon waves suggestive of ARVC
  - Left ventricular hypertrophy suggesting hypertrophic cardiomyopathy

ARVC = arrhythmogenic right ventricular cardiomyopathy; AV = atrioventricular; BBB = bundle branch block; b.p.m. = beats per minute; ECG = electrocardiogram; OH = orthostatic hypotension; VT = ventricular tachycardia.

The management of TLOC of suspected syncopal nature in the ED should answer the following three key questions:

1) Is there a serious underlying cause that can be identified?
2) What is the risk of a serious outcome?
3) Should the patient be admitted to hospital?

Figure 4 Management and risk stratification of patients referred to the Emergency Department (ED) for Transient Loss of Consciousness (TLOC) suspected to be syncope



[a]e.g. this includes pulmonary embolism presenting with shortness of breath, pleuritic chest pain, and syncope, but not trauma secondary to syncope.

Table 4 High-risk features (that suggest a serious condition) and low-risk features (that suggest a benign condition) in patients with syncope at initial evaluation in the ED

SYNCOPAL EVENT
Low-risk
• Associated with prodrome typical of reflex syncope (e.g. light-headedness, feeling of warmth, sweating, nausea, vomiting) • After sudden unexpected unpleasant sight, sound, smell, or pain • After prolonged standing or crowded, hot places • During a meal or postprandial • Triggered by cough, defaecation, or micturition • With head rotation or pressure on carotid sinus (e.g. tumour, shaving, tight collars) • Standing from supine/sitting position
High-risk
Major
• New onset of chest discomfort, breathlessness, abdominal pain, or headache • Syncope during exertion or when supine • Sudden onset palpitation immediately followed by syncope
Minor (high-risk only if associated with structural heart disease or abnormal ECG):
• No warning symptoms or short (<10 seconds) prodrome • Family history of SCD at young age • Syncope in the sitting position
PAST MEDICAL HISTORY
Low-risk
• Long history (years) of recurrent syncope with low–risk features with the samechar-acteristics of the current episode • Absence of structural heart disease
High-risk
Major
• Severe structural or coronary artery disease (heart failure, low LVEF or previ-ous myocardial infarction)
PHYSICAL EXAMINATION
Low-risk
• Normal examination
High-risk
Major
• Unexplained systolic BP in the ED <90 mmHg • Suggestion of gastrointestinal bleed on rectal examination • Persistent bradycardia (<40 b.p.m.) in awake state and in absence of physical train-ing • Undiagnosed systolic murmur

PHYSICAL EXAMINATION

Low-risk

- Normal examination

High-risk

Major

- Unexplained systolic BP in the ED <90 mmHg
- Suggestion of gastrointestinal bleed on rectal examination
- Persistent bradycardia (<40 b.p.m.) in awake state and in absence of physical training
- Undiagnosed systolic murmur

ECG[a]

Low-risk

- Normal ECG

High-risk

Major	**Minor** (high-risk only if history consistent with arrhythmic syncope)
• ECG changes consistent with acute ischaemia • Mobitz II second- and third-degree AV block • Slow AF (<40 b.p.m.) • Persistent sinus bradycardia (<40 b.p.m.), or repetitive sinoatrial block or sinus pauses >3 seconds in awake state and in absence of physical training • Bundle branch block, intraventricular conduction disturbance, ventricular hypertrophy, or Q waves consistent with ischaemic heart disease or cardiomyopathy • Sustained and non-sustained VT • Dysfunction of an implantable cardiac device (pacemaker or ICD) • Type 1 Brugada pattern • ST-segment elevation with type 1 morphology in leads V1–V3 (Brugada pattern) • QTc >460 ms in repeated 12-lead ECGs indicating LQTS	• Mobitz I second-degree AV block and first-degree AV block with markedly prolonged PR interval • Asymptomatic inappropriate mild sinus bradycardia (40–50 b.p.m.), or slow AF (40–50 b.p.m.) • Paroxysmal SVT or atrial fibrillation • Pre-excited QRS complex • Short QTc interval (≤340 ms) • Atypical Brugada patterns • Negative T waves in right precordial leads, epsilon waves suggestive of ARVC

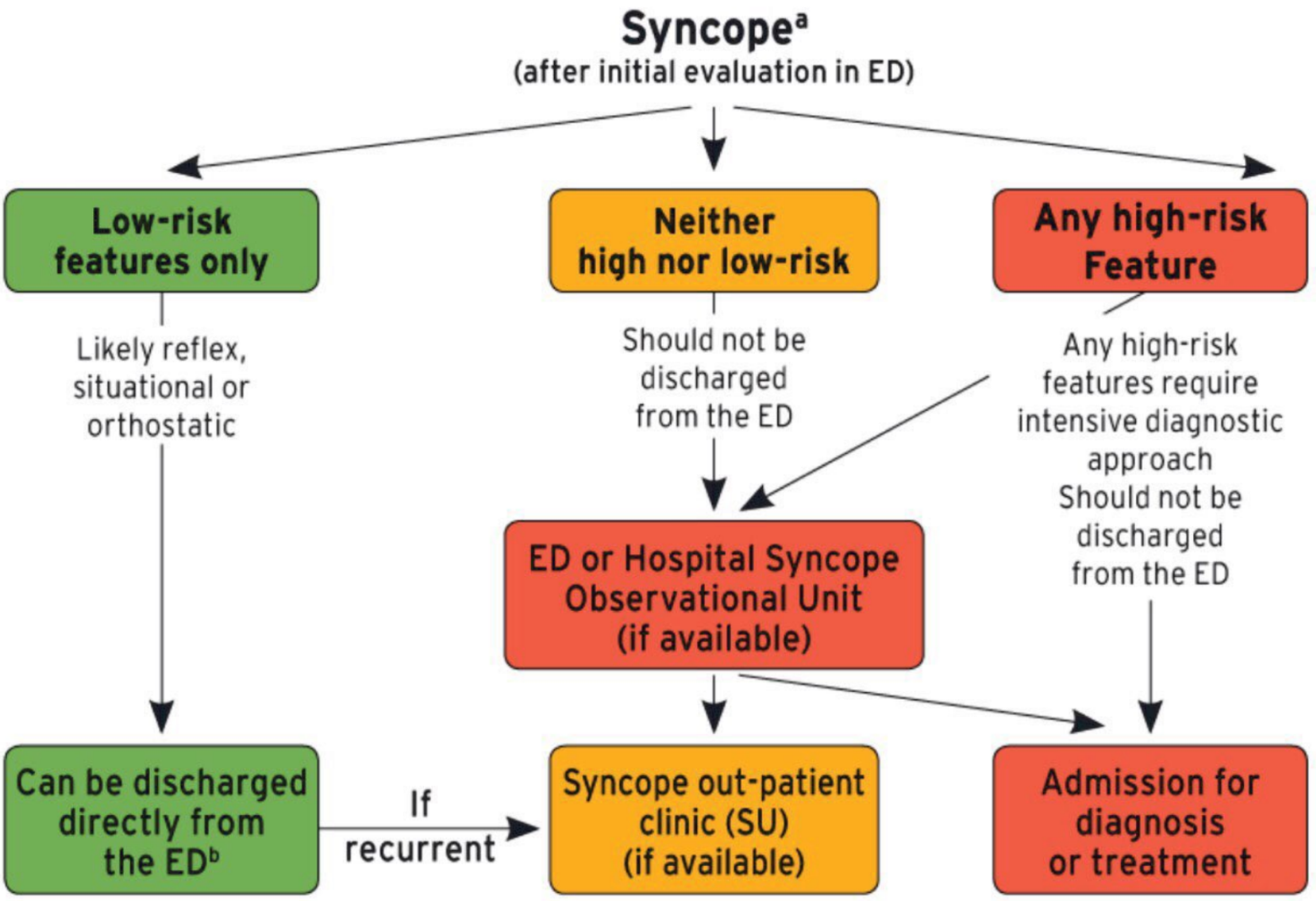
AF = atrial fibrillation; ARVC = arrhythmogenic right ventricular cardiomyopathy; AV = atrioventricular; BP = blood pressure; b.p.m. = beats per minute; ECG = electrocardiogram; ED = emergency department; ICD = implantable cardioverter defibrillator; LQTS = long QT syndrome; LVEF = left ventricular ejection fraction; SCD = sudden cardiac death; SVT = supraventricular tachycardia; VT = ventricular tachycardia.
[a]Some ECG criteria are per se diagnostic of the cause of the syncope (see recommendations: Diagnostic criteria); in such circumstances appropriate therapy is indicated without further investigations. We strongly suggest the use of standardized criteria to identify ECG abnormalities with the aim of precise diagnosis of ECG-defined cardiac syndromes in ED practice.

Patients with low-risk features: These patients do not need further diagnostic tests in the ED as they are likely to have reflex, situational, or orthostatic syncope. They may benefit from reassurance, or counselling.

Patients with high-risk features: These patients should be classified as HIGHRISK; they require an intensive diagnostic approach and may need urgent treatment and admission. These patients should be monitored (although it is unclear for how long this should be, most studies suggesting up to 6 hours in the ED and up to 24 hours in hospital) in a setting where resuscitation can be performed in case of deterioration.

Patients that have neither high- nor low-risk features: These patients will require expert syncope opinion, which can probably be safely managed in an outpatient setting. There is no direct evidence that admitting patients to hospital changes their outcome, whilst there is evidence that management in an ED observation unit and/or fast-track to a syncope outpatient unit is beneficial.

Figure 5 ED risk stratification flowchart. Low- and high-risk features are listed in Table 4



ED = emergency department; SU = syncope unit.
[a]Recent studies have suggested that outcomes in patients presenting with presyncope are similar to those presenting with syncope - [b]These patients may still require admission to hospital for associated illness, injury or welfare reasons. Low-risk patients can be referred to the outpatient syncope clinic for therapy purposes, if needed.

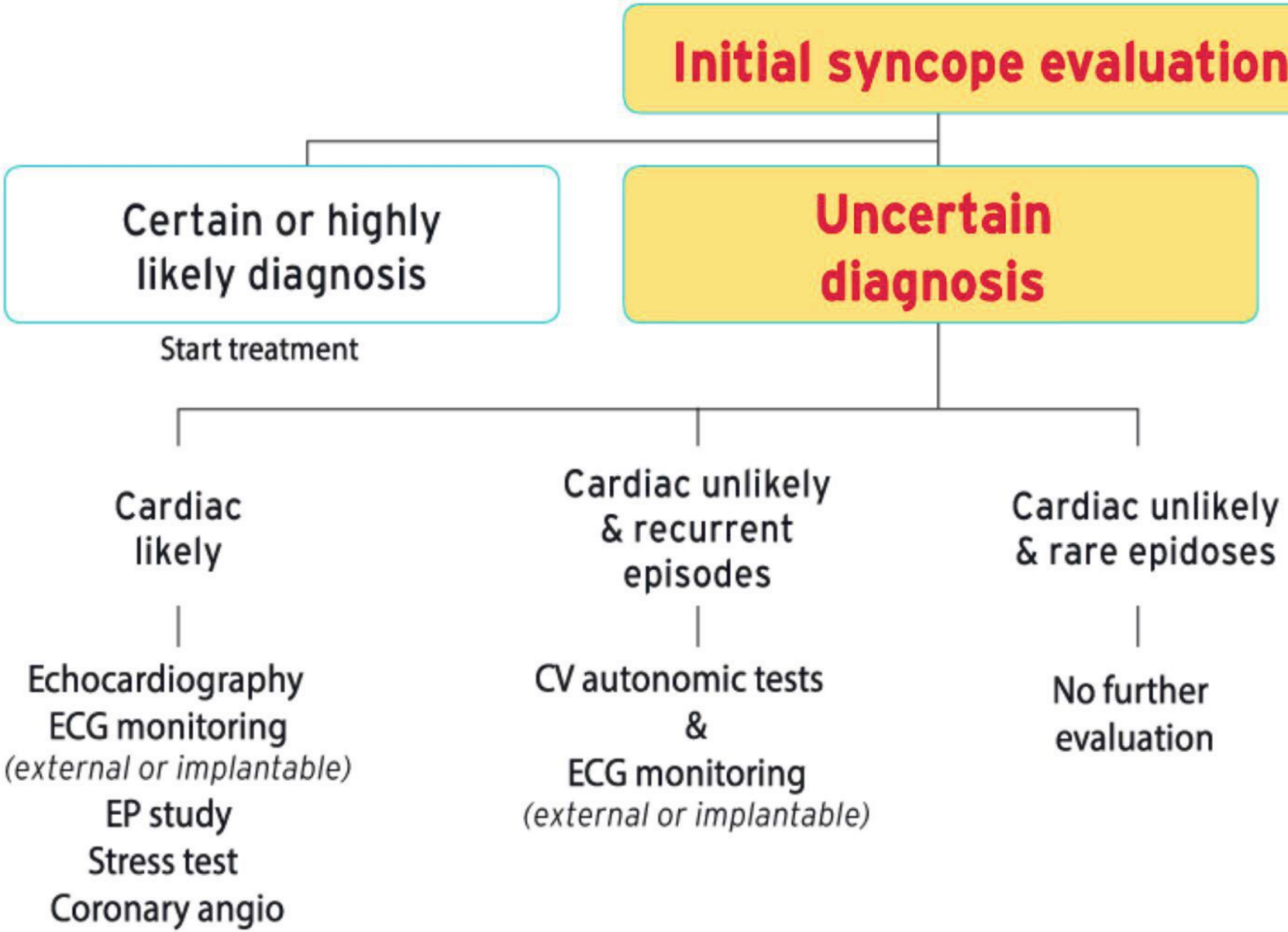
Whereas it is crucial to identify these high-risk patients to ensure early, rapid, and intensive investigation, not all patients at high-risk need hospitalization. This Task Force believes that the implementation of novel care pathways and organizational approaches such as ED observation units and syncope in- and outpatient units (Figure 5) offer safe and effective alternatives to admission for the cases listed in Table 5.

Table 5 High-risk syncope patients – criteria favouring stay in an ED observation unit and/or fast-track to syncope unit versus requiring admission to hospital

Favour initial management in ED observation unit and/or fast-track to syncope unit	Favour admission to hospital
High-risk features AND: • Stable, known structural heart disease • Severe chronic disease • Syncope during exertion • Syncope while supine or sitting • Syncope without prodrome • Palpitations at the time of syncope • Inadequate sinus bradycardia or sinoatrial block • Suspected device malfunction or inappropriate intervention • Pre-excited QRS complex • SVT or paroxysmal atrial fibrillation • ECG suggesting an inheritable arrhythmogenic disorders • ECG suggesting ARVC	**High-risk features AND:** • Any potentially severe coexisting disease that requires admission • Injury caused by syncope • Need of further urgent evaluation and treatment if it cannot be achieved in another way (i.e. observation unit), e.g. ECG monitoring, echocardiography, stress test, electrophysiological study, angiography, device malfunction, etc. • Need for treatment of syncope

ARVC = arrhythmogenic right ventricular cardiomyopathy; ECG = electrocardiogram; ED = emergency department; SVT = supraventricular tachycardia.

Figure 6 Diagnostic strategy when the initial evaluation is unable to establish a diagnosis



EEG = electroencephalogram; EP = electrophysiological.

- History of syncope and its reproduction by CSM defines CSS; positive CSM without a history of syncope defines carotid sinus hypersensitivity. Carotid sinus hypersensitivity in patients with unexplained syncope may be a non-specific finding because it is present in up to 40% of older populations and should be used with caution for diagnosis of the mechanism of syncope.
- CSM should be performed with the patient in the supine and upright positions and with continuous beat-to-beat BP monitoring. This may be more readily performed in the tilt laboratory.
- Albeit neurological complications are very rare, the risk of provocation of TIA with the massage suggests that CSM should be undertaken with caution in patients with previous TIA, stroke, or known carotid stenosis >70%.

Carotid sinus massage

Recommendations	Class[a]	Level[b]
Indications CSM is indicated in patients >40 years of age with syncope of unknown origin compatible with a reflex mechanism.	I	B
Diagnostic criteria CSS is confirmed if CSM causes bradycardia (asystole) and/or hypotension that reproduce spontaneous symptoms and patients have clinical features compatible with a reflex mechanism of syncope.	I	B

BP = blood pressure; CSM = carotid sinus massage; CSS = carotid sinus syndrome.
[a]Class of recommendation
[b]Level of evidence.

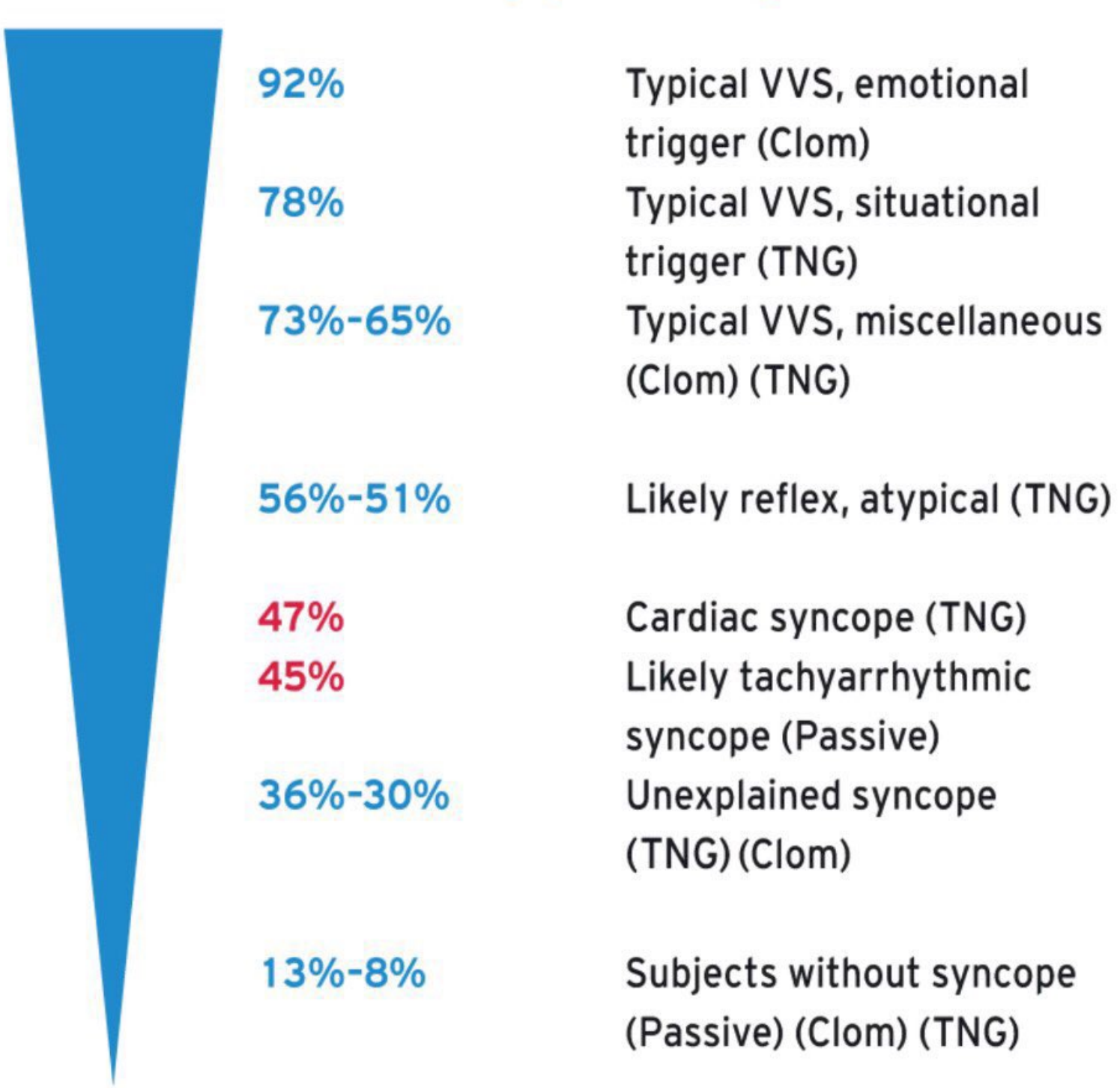
Active standing		
Recommendations	**Class[a]**	**Level[b]**
Indications		
Intermittent determination by sphygmomanometer of BP and HR while supine and during active standing for 3 minutes are indicated at initial syncope evaluation.	I	C
Continuous beat-to-beat non-invasive BP and HR measurement may be preferred when short-lived BP variations are suspected such as in initial OH.	IIb	C
Diagnostic criteria		
Syncope due to OH is confirmed when there is a fall in systolic BP from baseline value ≥20 mmHg or diastolic BP ≥10 mmHg or a decrease in systolic BP to <90 mmHg that reproduces spontaneous symptoms.	I	C
Syncope due to OH should be considered likely when there is an asymptomatic fall in systolic BP from baseline value ≥20 mmHg or diastolic BP ≥10 mmHg or a decrease in systolic BP to <90 mmHg and symptoms (from history) are consistent with OH.	IIa	C
Syncope due to OH should be considered likely when there is a symptomatic fall in systolic BP from baseline value ≥20 mmHg or diastolic BP ≥10 mmHg or a decrease in systolic BP to <90 mmHg and not all of the features (from history) are suggestive of OH.	IIa	C
POTS should be considered likely when there is an orthostatic HR increase (>30 b.p.m. or to >120 b.p.m. within 10 minutes of active standing) in the absence of OH that reproduces spontaneous symptoms.	IIa	C
Syncope due to OH may be considered possible when there is an asymptomatic fall in systolic BP from baseline value ≥20 mmHg or diastolic BP ≥10 mmHg or a decrease in systolic BP to <90 mmHg and symptoms (from history) are less consistent with OH.	IIb	C

BP = blood pressure; b.p.m. = beats per minute; OH = orthostatic hypotension; HR = heart rate; POTS = posturalorthostatic tachycardia syndrome.
[a]Class of recommendation - [b]Level of evidence

Active standing		
Recommendations	**Class[a]**	**Level[b]**
Indications		
Tilt testing should be considered in patients with suspected reflex syncope, OH, POTS, or PPS.	IIa	B
Tilt testing may be considered to educate patients to recognize symptoms and learn physical manoeuvres.	IIb	B
Diagnostic criteria		
Reflex syncope, OH, POTS, or PPS should be considered likely if tilt testing reproduces symptoms along with the characteristic circulatory pattern of these conditions.	IIa	B

EEG = electroencephalogram; OH = orthostatic hypotension; POTS = postural orthostatic tachycardia syndrome; PPS = psychogenic pseudosyncope; VVS = vasovagal syncope.
[a]Class of recommendation - [b]Level of evidence

Figure 7 Rates of tilt testing positivity in different clinical conditions.
Tilt testing has an acceptable sensitivity and specificity when these are calculated in patients with true VVS or without a history of syncope. However, there is an inability to apply the test to populations with syncope of uncertain cause where it is hoped tilt testing might prove decisive. In other words, tilt testing offers little diagnostic value in patients for whom it is most needed. In these patients, a positive tilt test reveals a susceptibility to orthostatic stress.



Clom = clomipramine; TNG = trinitroglycerin; VVS = vasovagal syncope.

Basic autonomic function tests		
Recommendations	**Class[a]**	**Level[b]**
Valsalva manoeuvre		
Valsalva manoeuvre should be considered for assessment of autonomic function in patients with suspected neurogenic OH.	IIa	B
Valsalva manoeuvre may be considered for confirming the hypotensive tendency induced by some forms of situational syncope, e.g. cough, brass instrument playing, singing and weight lifting.	IIb	C
Deep breathing test		
Deep breathing test should be considered for assessment of autonomic function in patients with suspected neurogenic OH.	IIa	B
Other autonomic function tests		
Other autonomic function tests (30:15 ratio, cold pressure test, sustained hand grip test, and mental arithmetic test) may be considered for assessment of autonomic function in patients with suspected neurogenic OH.	IIb	C
ABPM		
ABPM is recommended to detect nocturnal hypertension in patients with autonomic failure.	I	B
ABPM should be considered to detect and monitor degree of OH and supine hypertension in daily life in patients with autonomic failure.	IIa	C
ABPM and HBPM may be considered to detect whether BP is abnormally low during episodes suggestive of orthostatic intolerance.	IIb	C

Electrocardiographic monitoring		
Recommendations	**Class[a]**	**Level[b]**
Indications		
Immediate in-hospital monitoring (in bed or by telemetry) is indicated in high-risk patients (defined in Table 4).	I	C
Holter monitoring should be considered in patients who have frequent syncope or presyncope (≥1 episode per week).	IIa	B
External loop recorders should be considered, early after the index event, in patients who have an inter-symptom interval ≤4 weeks.	IIa	B
ILR: *ILR* is indicated in an early phase of evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria (listed in Table 4), and a high likelihood of recurrence within the battery life of the device.	I	A
ILR is indicated in patients with high-risk criteria (listed in Table 5) in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment and who do not have conventional indications for primary prevention ICD or pacemaker indication.	I	A
ILR should be considered in patients with suspected or certain reflex syncope presenting with frequent or severe syncopal episodes.	IIa	B
ILR may be considered in patients in whom epilepsy was suspected but the treatment has proven ineffective.	IIb	B
ILR may be considered in patients with unexplained falls.	IIb	B
Diagnostic criteria		
Arrhythmic syncope is confirmed when a correlation between syncope and an arrhythmia (bradyarrhythmia or tachyarrhythmia) is detected.	I	B
In the absence of syncope, arrhythmic syncope should be considered likely when periods of Mobitz II second- or third-degree AV block or a ventricular pause >3 seconds (with possible exception of young trained persons, during sleep or rate-controlled atrial fibrillation), or rapid prolonged paroxysmal SVT or VT are detected.	IIa	C

AV = atrioventricular; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SVT = supraventricular tachycardia; VT = ventricular tachycardia.

[a]Class of recommendation - [b]Level of evidence.

ing with frequent or severe syncopal episodes.	IIa	B
ILR may be considered in patients in whom epilepsy was suspected but the treatment has proven ineffective.	IIb	B
ILR may be considered in patients with unexplained falls.	IIb	B
Diagnostic criteria		
Arrhythmic syncope is confirmed when a correlation between syncope and an arrhythmia (bradyarrhythmia or tachyarrhythmia) is detected.	I	B
In the absence of syncope, arrhythmic syncope should be considered likely when periods of Mobitz II second- or third-degree AV block or a ventricular pause >3 seconds (with possible exception of young trained persons, during sleep or rate-controlled atrial fibrillation), or rapid prolonged paroxysmal SVT or VT are detected.	IIa	C

AV = atrioventricular; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SVT = supraventricular tachycardia; VT = ventricular tachycardia.

[a]Class of recommendation - [b]Level of evidence.

Additional advice and clinical perspectives.

- Be aware that the pretest selection of the patients influences the subsequent findings. Include patients with a high likelihood of arrhythmic events. The duration (and technology) of monitoring should be selected according to the risk and the predicted recurrence rate of syncope.
- Exclude patients with a clear indication for ICD, pacemaker, or other treatments independent of a definite diagnosis of the cause of syncope.
- Include patients with a high probability of recurrence of syncope in a reasonable time. Owing to the unpredictability of syncope recurrence, be prepared to wait for up to 4 years before obtaining such a correlation.
- In the absence of a documented arrhythmia, presyncope cannot be considered a surrogate for syncope, whereas the documentation of a significant arrhythmia at the time of presyncope can be considered a diagnostic finding.
- The absence of arrhythmia during syncope excludes arrhythmic syncope.

Video recording in suspected syncope

Recommendations	Class[a]	Level[b]
Home video recordings of spontaneous events should be considered. Physicians should encourage patients and their relatives to obtain home video recordings of spontaneous events	IIa	C
Adding video recording to tilt testing may be considered in order to increase reliability of clinical observation of induced events.	IIb	C

[a]Class of recommendation - [b]Level of evidence.

In recent years, the development of powerful non-invasive methods, i.e. prolonged ECG monitoring, showing a higher diagnostic value, has decreased the importance of EPS as a diagnostic test. Nevertheless, EPS remains useful for diagnosis in the following specific clinical situations: asymptomatic sinus bradycardia (suspected sinus arrest causing syncope), bifascicular BBB (impending high-degree AV block), and suspected tachycardia.

- In general, whereas a positive EPS predicts the cause of syncope, a negative study is unable to exclude an arrhythmic syncope and further evaluation is warranted.
- The induction of polymorphic VT or VF in patients with ischaemic or DCM cannot be considered a diagnostic finding of the cause of syncope.
- EPS is generally not useful in patients with syncope, normal ECG, no heart disease, and no palpitations.

Electrophysiological study

Recommendations	Class[a]	Level[b]
Indications		
In patients with syncope and previous myocardial infarction or other scar-related conditions, EPS is indicated when syncope remains unexplained after non-invasive evaluation.	I	B
In patients with syncope and bifascicular BBB, EPS should be considered when syncope remains unexplained after non-invasive evaluation.	IIa	B
In patients with syncope and asymptomatic sinus bradycardia, EPS may be considered in a few instances when non-invasive tests (e.g. ECG monitoring) have failed to show a correlation between syncope and bradycardia.	IIb	B
In patients with syncope preceded by sudden and brief palpitations, EPS may be considered when syncope remains unexplained after non-invasive evaluation.	IIb	C
EPS-guided therapy		
In patients with unexplained syncope and bifascicular BBB, a pacemaker is indicated in the presence of either a baseline H-V interval of ≥70 ms, or second- or third-degree His-Purkinje block during incremental atrial pacing, or with pharmacological challenge.	I	B
In patients with unexplained syncope and previous myocardial infarction or other scar-related conditions, it is recommended to manage induction of sustained monomorphic VT according to the current ESC Guidelines for VA.	I	B
In patients without structural heart disease with syncope preceded by sudden and brief palpitations, it is recommended to manage the induction of rapid SVT or VT, which reproduces hypotensive or spontaneous symptoms, with appropriate therapy according to the current ESC Guidelines.	I	C
In patients with syncope and asymptomatic sinus bradycardia, a pacemaker should be considered if a prolonged corrected SNRT is present.	IIa	B

- For patients without suspected cardiac disease after history taking, physical examination, and electrocardiography, the echocardiogram does not provide additional useful information, suggesting that syncope alone is not an indication for echocardiography.
- Computed tomography or magnetic resonance imaging should be considered in selected patients presenting with syncope of suspected cardiac structural origin when echocardiography is not diagnostic.

Echocardiography

Recommendations	Class[a]	Level[b]
Indications		
Echocardiography is indicated for diagnosis and risk stratification in patients with suspected structural heart disease.	I	B
Two-dimensional and Doppler echocardiography during exercise in the standing, sitting, or semi-supine position to detect provocable left ventricular outflow tract obstruction is indicated in patients with HCM, a history of syncope, and a resting or provoked peak instantaneous left ventricular outflow tract gradient <50 mmHg.	I	B
Diagnostic criteria		
Aortic stenosis, obstructive cardiac tumours or thrombi, pericardial tamponade, and aortic dissection are the most probable causes of syncope when the echocardiogram shows the typical features of these conditions.	I	C

HCM = hypertrophic cardiomyopathy.
[a]Class of recommendation - [b]Level of evidence.

There are no data supporting routine exercise testing in patients with syncope.

Echocardiography		
Recommendations	**Class[a]**	**Level[b]**
Indications		
Exercise testing is indicated in patients who experience syncope during or shortly after exertion.	I	C
Diagnostic criteria		
Syncope due to second- or third-degree AV block is confirmed when the AV block develops during exercise, even without syncope.	I	C
Reflex syncope is confirmed when syncope is reproduced immediately after exercise in the presence of severe hypotension.	I	C

AV = atrioventricular.

[a]Class of recommendation - [b]Level of evidence.

In patients presenting with syncope and obstructive coronary artery disease, percutaneous coronary intervention was not associated with significant reduction in readmission for syncope. Angiography alone is not diagnostic of the cause of syncope.

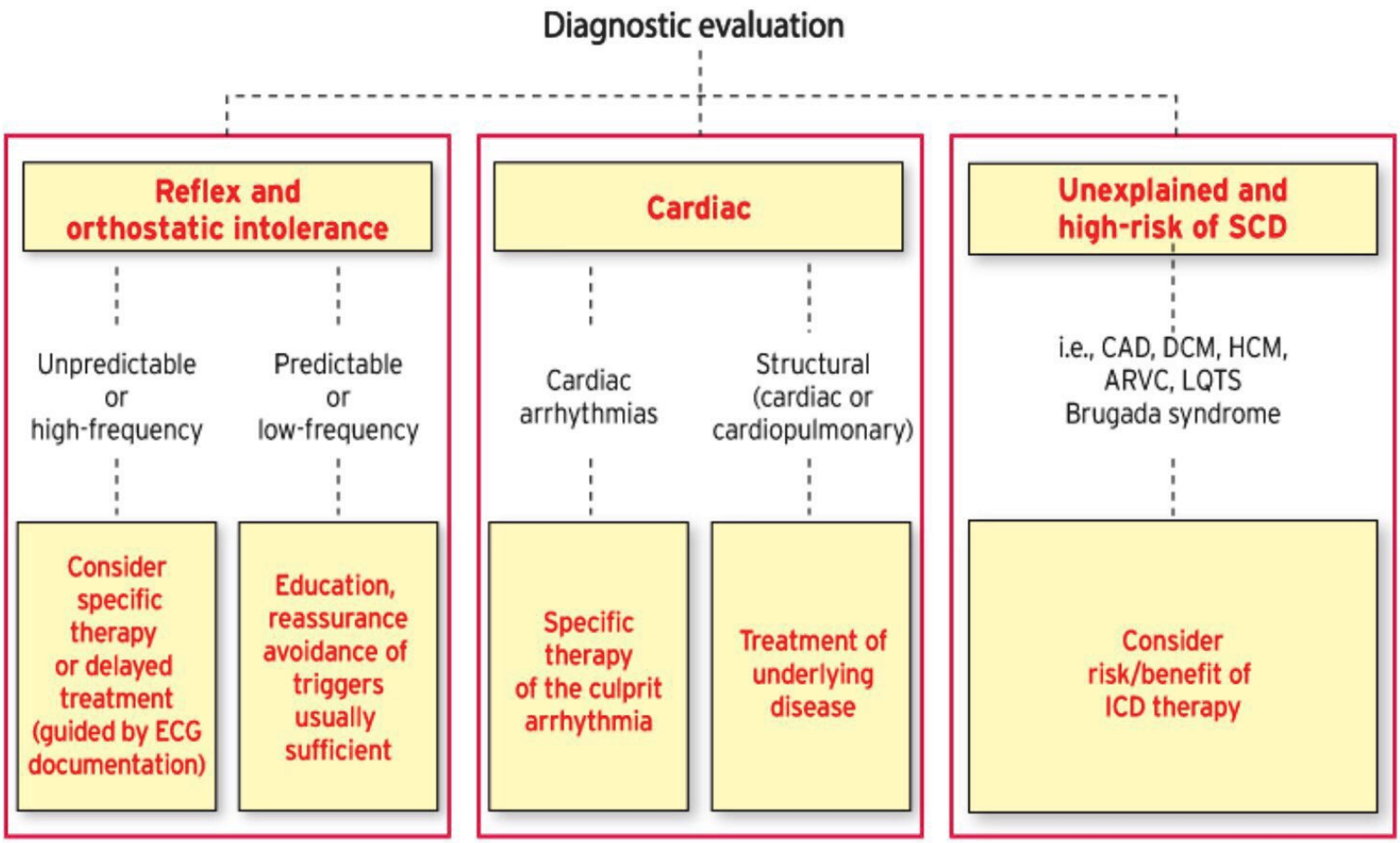
Echocardiography		
Recommendations	**Class[a]**	**Level[b]**
Indications		
In patients with syncope, the same indications for coronary angiography should be considered as in patients without syncope.	IIa	C

[a]Class of recommendation - [b]Level of evidence.

The general, framework of treatment is based on risk stratification and identification of specific mechanisms when possible (Figure 8).

- The efficacy of therapy aimed at preventing syncope recurrence is largely determined by the mechanism of syncope rather than its aetiology. Bradycardia is a frequent mechanism of syncope. Cardiac pacing is the most powerful therapy of bradycardia but its efficacy is less if hypotension coexists.
- Often, therapy to prevent recurrence differs from that for the underlying disease. The management of patients at high risk of SCD requires careful assessment of the individual patient's risk.

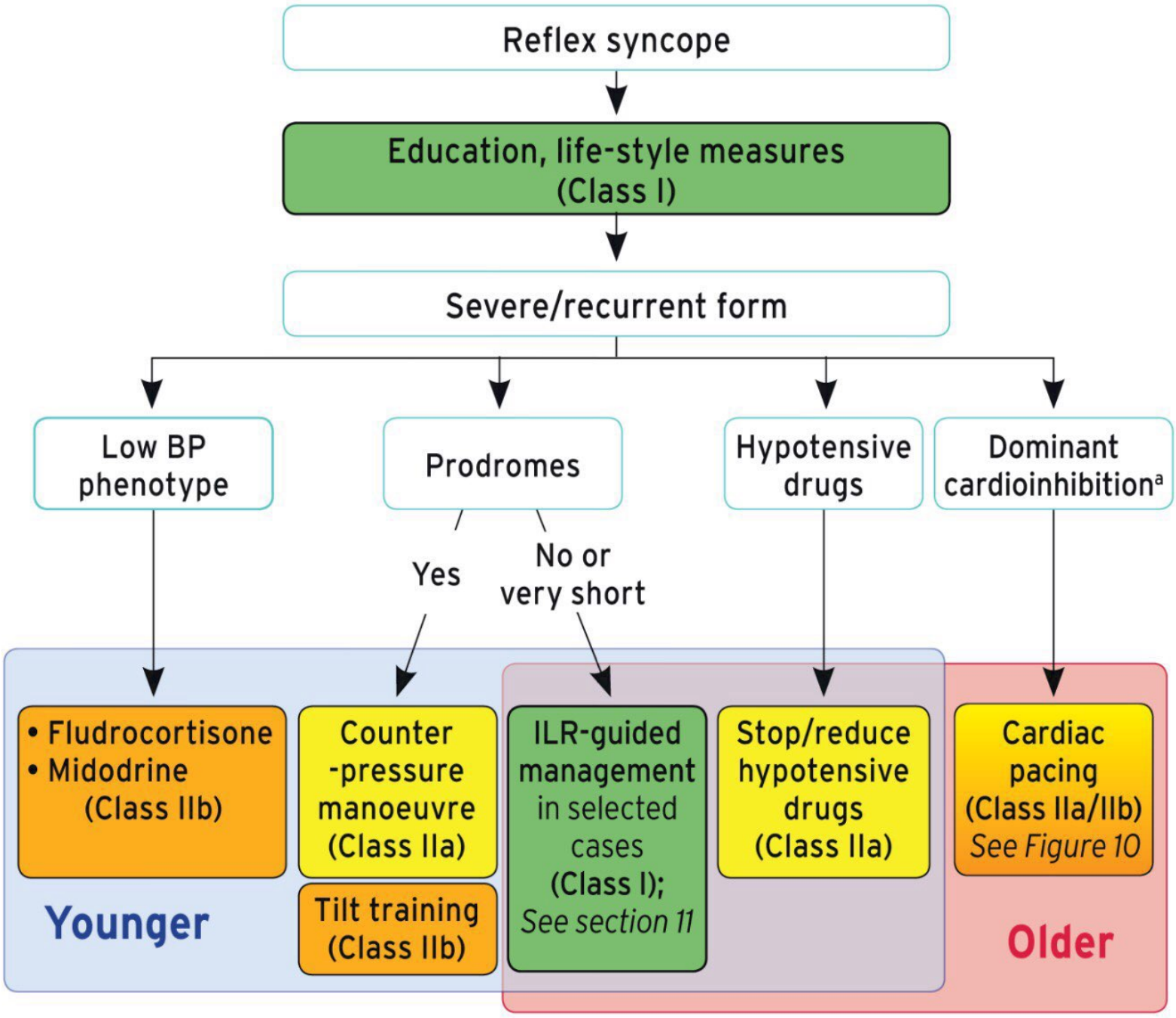
Figure 8. General framework of treatment is based on risk stratification and identification of specific mechanisms when possible



ARVC = arrhythmogenic right ventricular cardiomyopathy; CAD = coronary artery disease; DCM = dilated cardiomyopathy; ECG = electrocardiographic; HCM= hypertrophic cardiomyopathy; ICD = implantable cardioverter defibrillator; LQTS = longQT syndrome; SCD= sudden cardiac death.

Despite its benign course, recurrent and unpredictable reflex syncope may be disabling. The cornerstone of management of these patients is a nonpharmacological treatment, including education, lifestyle modification, and reassurance regarding the benign nature of the condition. Additional treatment may be necessary in patients with severe forms, in particular: when very frequent syncope alters quality of life; when recurrent syncope without – or with a very short – prodrome exposes the patient to a risk of trauma; and when syncope occurs during a high-risk activity (Figure 9).

Figure 9. Schematic practical decision pathway for the first-line management of reflex syncope (based on patient's history and tests) according to age, severity of syncope, and clinical forms



ILR = implantable loop recorder.
[a]Spontaneous or provoked by, sequentially, carotid sinus massage, tilt testing, or ILR.

Remark to figure 9:

- The duration of prodrome is largely subjective and imprecise. In practice, the prodrome is ‘absent or very short’ if it does not allow patients enough time to act, such as to sit or lie down. In general, this time is 5-10 s.
- *“low BP phenotype”* identifies patients with chronic low BP values (in general, systolic around 110 mmHg who have a clear history of orthostatic intolerance and orthostatic VVS).
- *“dominant cardioinhibition”* identifies patients in whom clinical features and results of tests suggest that sudden cardioinhibition is mainly responsible for syncope. One such clue is lack of prodromes.
- Overlap between subgroups and exceptions are expected.

Treatment of reflex syncope		
Recommendations	**Class[a]**	**Level[b]**
Education and lifestyle modifications		
Explanation of the diagnosis, provision of reassurance, explanation of risk of recurrence, avoidance of triggers and situations are indicated in all patients	I	B
Discontinuation/reduction of hypotensive therapy		
Modification or discontinuation of hypotensive drug regimen should be considered in patients with vasodepressor syncope, if possible.	IIa	B
Physical manoeuvres		
Isometric PCM should be considered in patients with prodromes who are less than 60 years of age.	IIa	B
Tilt training may be considered for the education of young patients.	IIb	B
Pharmacological therapy		
Fludrocortisone may be considered in young patients with the orthostatic form of VVS, low-normal values of arterial BP, and absence of contraindication to the drug.	IIb	B
Midodrine may be considered in patients with the orthostatic form of VVS.	IIb	B
Beta-adrenergic blocking drugs are not indicated.	III	A
Cardiac pacing		
Cardiac pacing should be considered to reduce syncopal recurrences in patients aged >40 years, with spontaneous documented symptomatic asystolic pause/s >3 seconds or asymptomatic pause/s >6 seconds due to sinus arrest or AV block or the combination of the two.	IIa	B
Cardiac pacing should be considered to reduce syncope recurrence in patients with cardioinhibitory carotid sinus syndrome who are >40 years with recurrent frequent unpredictable syncope.	IIa	B
Cardiac pacing may be considered to reduce syncope recurrences in patients with tilt-induced asystolic response who are >40 years with recurrent frequent unpredictable syncope.	IIb	B
Cardiac pacing may be considered to reduce syncope recurrences in patients with the clinical features of adenosine-sensitive syncope.	IIb	B
Cardiac pacing is not indicated in the absence of a documented cardioinhibitory reflex.	III	B

AV = atrioventricular; BP = blood pressure; PCM = physical counter-pressure manoeuvres; VVS = vasovagal syncope.

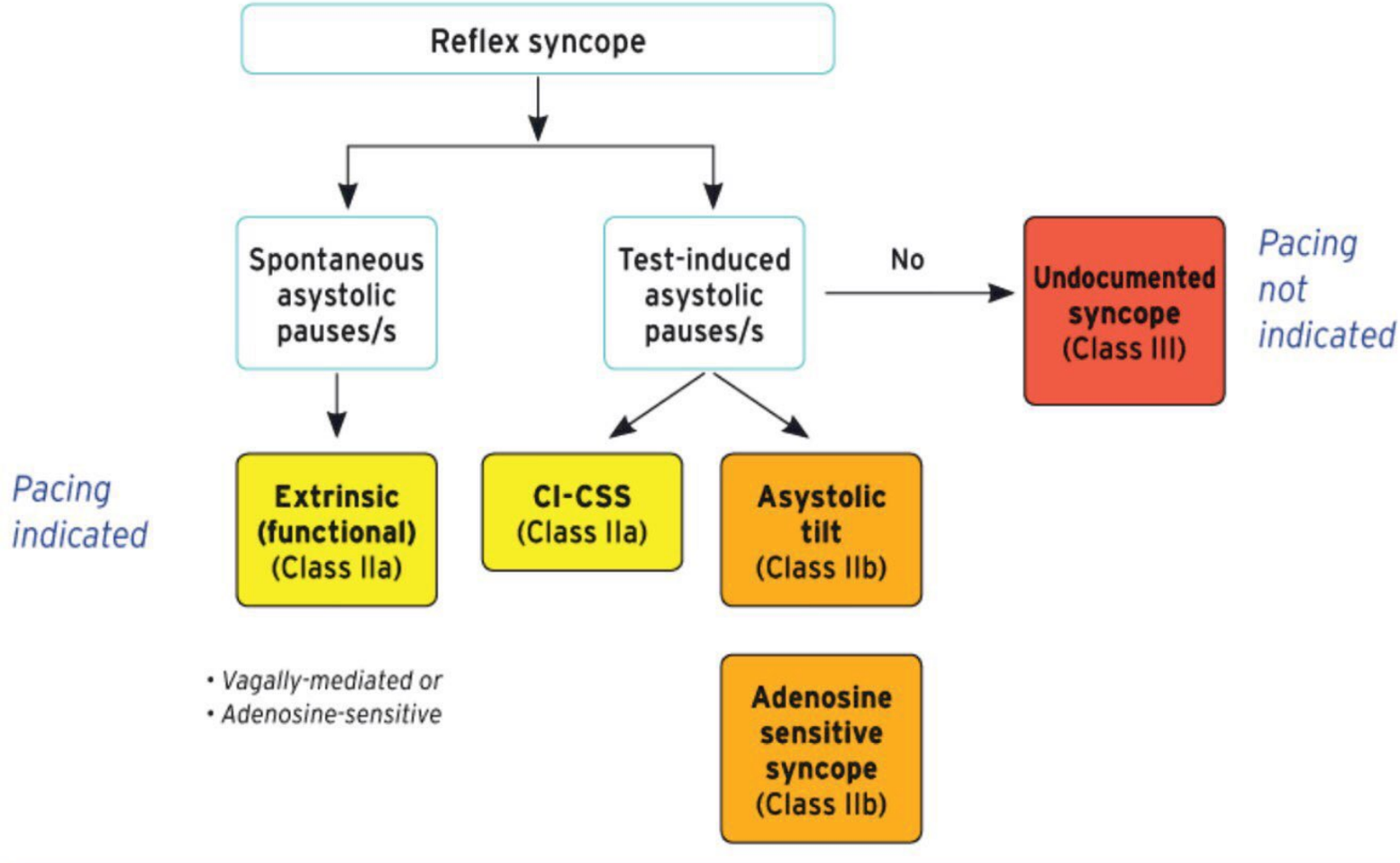
[a]Class of recommendation - [b]Level of evidence.

- In general, no therapy can completely prevent syncope recurrence during long term follow-up. A decrease of the syncope burden is a reasonable goal of therapy.
- In general, more than 50% of patients with recurrent syncopal episodes in the 1 or 2 years before evaluation do not have syncopal recurrences in the following 1 or 2 years and, in those with recurrences, the burden of syncope decreases even
more than 70% compared with the preceding period. The effect of education and reassurance is probably the most likely reason for the decrease in syncope after diagnostic evaluation.
- There is moderate evidence that discontinuation/reduction of hypotensive therapy targeting a systolic BP of 140 mmHg should be effective in reducing syncopal recurrences in patients with hypotensive susceptibility.
- Fludrocortisone, by increasing renal sodium re-absorption and expanding plasma volume, may counteract the physiological cascade leading to the orthostatic vasovagal reflex. Fludrocortisone should be titrated at a dosage from 0.05 to 0.2 mg once per day. The clinical benefit of fludrocortisone therapy should be balanced with the potential side effects of the drug.
- Midodrine (usually 2.5–10 mg, three times daily) has proved effective in small studies but none satisfied the criteria of a pivotal clinical trial. The most frequent side-effects that led to discontinuation of midodrine is supine hypertension, pilomotor reactions, and urinary problems (urinary retention, hesitancy, or urgency). The major limitation of midodrine is frequent dosing, limiting long-term compliance.

Permanent pacemaker therapy may be effective if asystole is a dominant feature of reflex syncope. Establishing a relationship between symptoms and bradycardia should be the goal of the clinical evaluation of patients with syncope and a normal baseline ECG. The efficacy of pacing depends on the clinical setting.

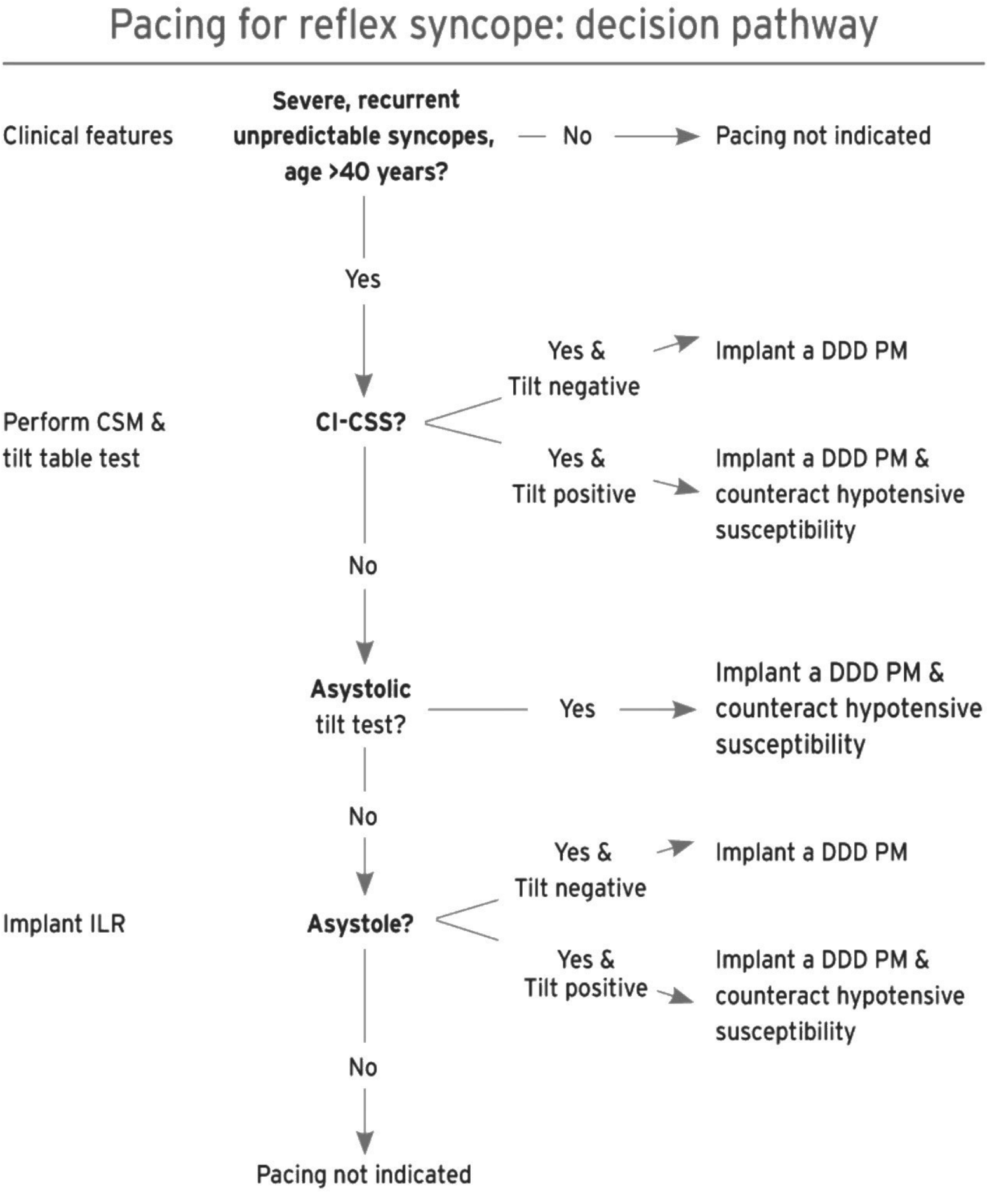
- The fact that pacing may be effective does not mean that it is also always necessary. It must be emphasized that the decision to implant a pacemaker needs to be made in the clinical context of a benign condition that frequently affects young patients. Thus, cardiac pacing should be limited to a highly selected small proportion of patients affected by severe reflex syncope. Patients suitable for cardiac pacing are older with a history of recurrent syncope beginning in middle or older age and with frequent injuries, probably due to presentation without warning. Syncope recurrence is still expected to occur despite cardiac pacing in a minority of patients.
- Tilt test response is the strongest predictor of pacemaker efficacy. Patients with negative tilt test will have a risk of recurrence of syncope as low as that observed in patients paced for intrinsic AV block. On the contrary, patients with a positive tilt test will have a higher risk of recurrence of syncope with a large confidence range, which makes any estimate of the benefit of pacing uncertain.

Figure 10. Summary of indications for pacing in patients with reflex syncope



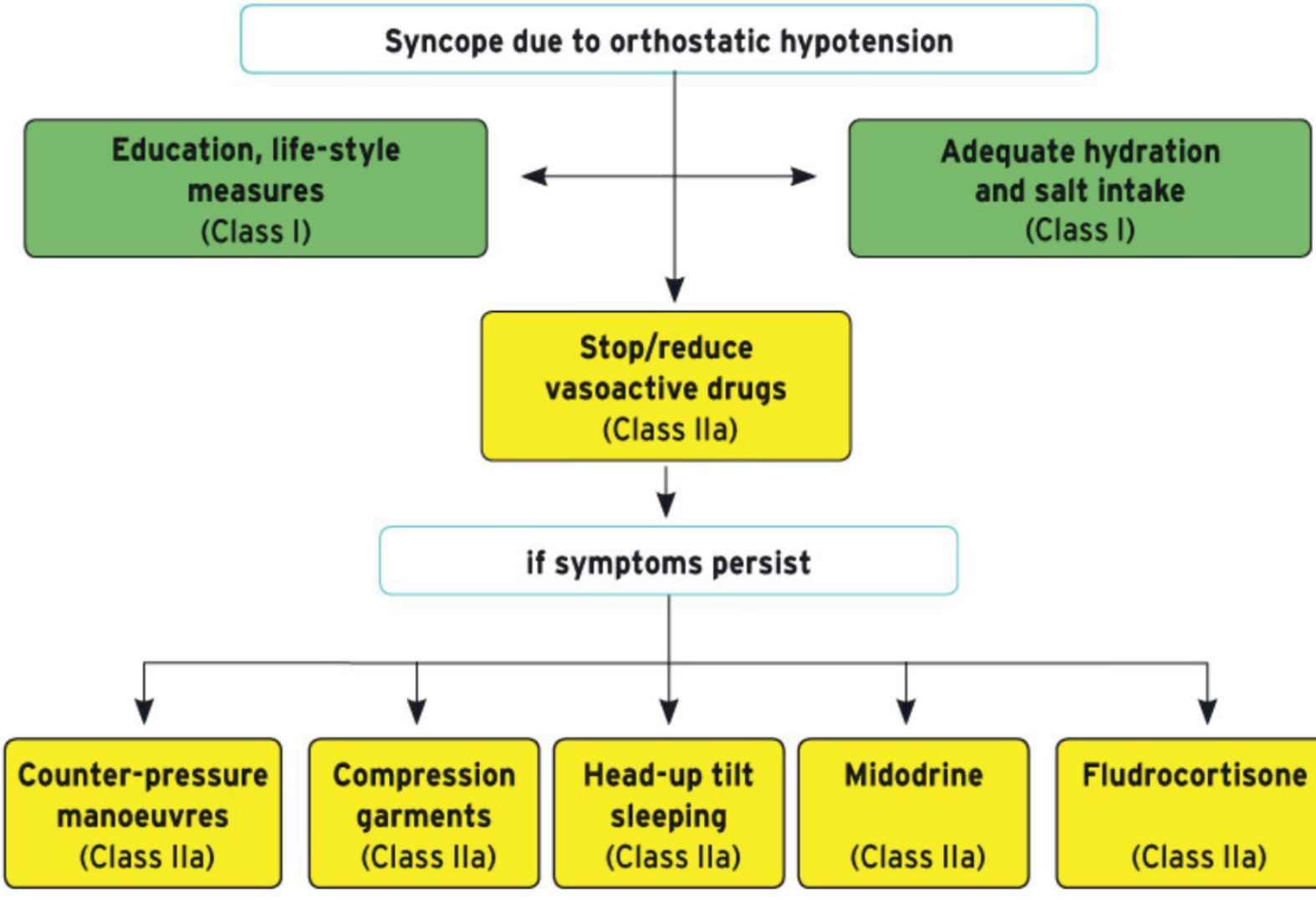
CI-CSS = cardioinhibitory carotid sinus syndrome.

Figure 11. Decision pathway for cardiac pacing in patients with reflex syncope



CI-CSS = cardioinhibitory carotid sinus syndrome; CSM = carotid sinusmassage; DDD PM = dual-chamber pacemaker; ILR = implantable loop recorder.

Figure 12 Schematic practical guide for treatment of orthostatic hypotension



- In individuals with established OH and risk factors for falls, aggressive BPlowering treatment should be avoided; their treatment targets should be revised to a systolic BP value of 140–150 mmHg and medication withdrawa should be considered.
- The *BP-lowering agents* (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and calcium-channel blockers) should be used preferentially, especially among patients at high-risk of falls, as diuretics an beta-blockers are associated with OH and falls and should be avoided in at risk individuals.
- Expansion of extracellular volume is an important goal. In the absence of hypertension, patients should be instructed to have a sufficient salt and water intake, targeting 2–3 litres of fluids per day and 10 grams of sodium chloride.
- *Midodrine* (2.5–10 mg, three times daily) was shown to be effective in randomized trials. The desirable effects of midodrine outweigh the undesirable effects.
- *Fludrocortisone* (0.1–0.3 mg once daily) was shown to be effective in randomized trial. The desirable effects of fludrocortisone outweigh the undesirable effects.

glotensin receptor blockers, and calcium-channel blockers) should be used preferentially, especially among patients at high-risk of falls, as diuretics and beta-blockers are associated with OH and falls and should be avoided in at-risk individuals.

- Expansion of extracellular volume is an important goal. In the absence of hypertension, patients should be instructed to have a sufficient salt and water intake, targeting 2–3 litres of fluids per day and 10 grams of sodium chloride.
- *Midodrine* (2.5–10 mg, three times daily) was shown to be effective in randomized trials. The desirable effects of midodrine outweigh the undesirable effects.
- *Fludrocortisone* (0.1–0.3 mg once daily) was shown to be effective in randomized trial. The desirable effects of fludrocortisone outweigh the undesirable effects.

Treatment of orthostatic hypotension

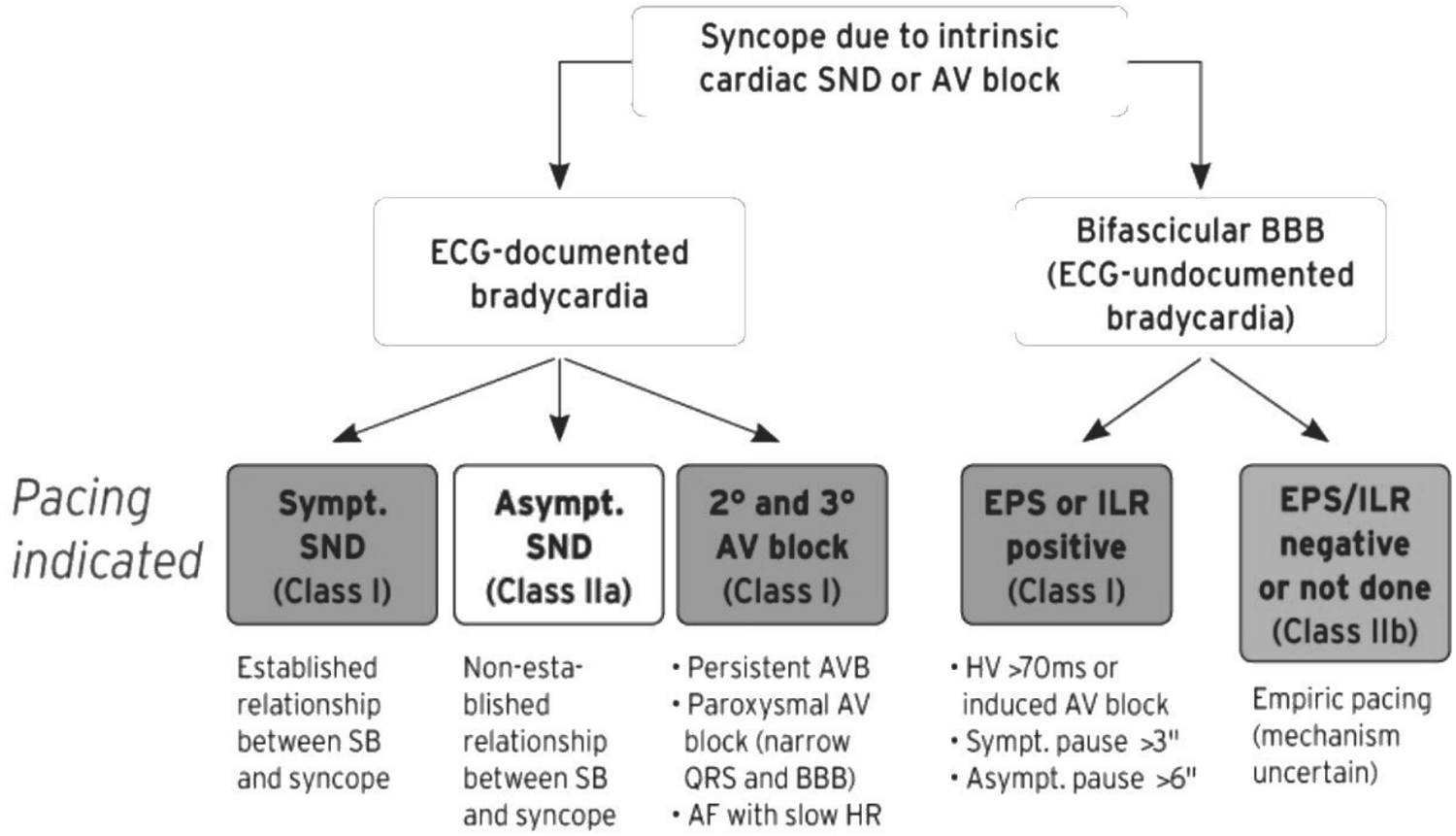
Recommendations	Class[a]	Level[b]
Explanation of the diagnosis, provision of reassurance, explanation of risk of recurrence, and avoidance of triggers and situations are indicated in all patients.	I	C
Adequate hydration and salt intake are indicated.	I	C
Modification or discontinuation of hypotensive drugs regimen should be considered.	IIa	B
Isometric PCM should be considered.	IIa	C
Abdominal binders and/or support stockings to reduce venous pooling should be considered.	IIa	B
Head-up tilt sleeping (>10 degrees) to increase fluid volume should be considered.	IIa	C
Midodrine should be considered if symptoms persist.	IIa	B
Fludrocortisone should be considered if symptoms persist.	IIa	C

PCM = physical counter-pressure manoeuvres.

[a]Class of recommendation

[b]Level of evidence.

Figure 13 Summary of indications for pacing in patients with syncope due to intrinsic cardiac bradycardia



AF = atrial fibrillation; asympt. = asymptomatic; AV = atrioventricular; BBB = bundle branch block; ECG = electrocardiogram; EPS = electrophysiological study; HR = heart rate; ILR = implantable loop recorder; SB = sinus bradycardia; SND = sinus node dysfunction; sympt. = symptomatic.

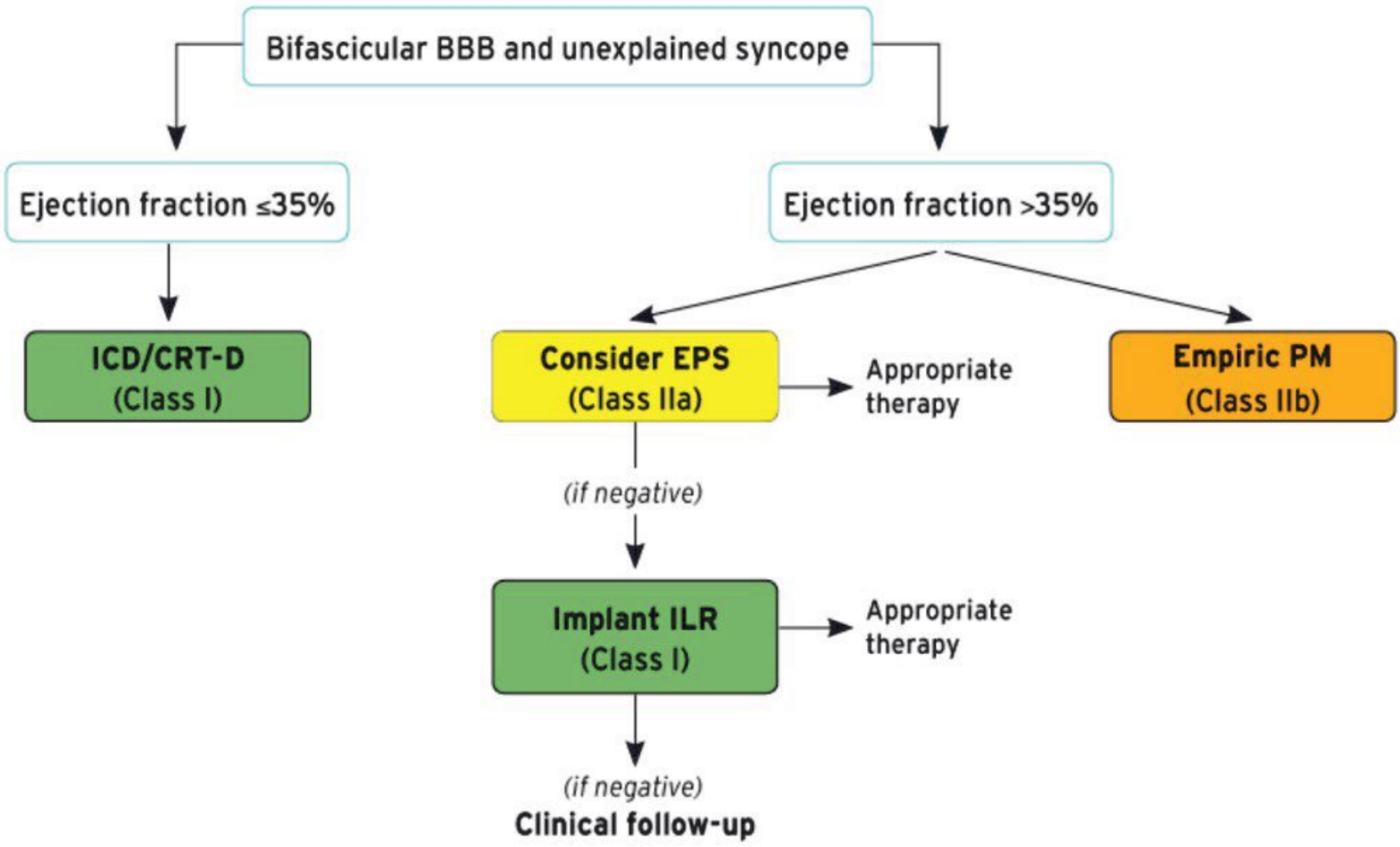
For interactivity see here

- In patients with sinus node disease, cardiac pacing is effective and useful for symptom relief when the correlation between symptoms and ECG is established, When the correlation between symptoms and ECG is not established, cardiac pacing may be reasonable in patients with documentation of asymptomatic pause/s.
- Cardiac pacing is the treatment of syncope associated with symptomatic AV block.
- Pacing is not indicated in unexplained syncope without evidence of any conduction disturbance.

Bifascicular BBB and syncope

- Less than half of the patients with bifascicular BBB and syncope have a final diagnosis of cardiac syncope, albeit the probability is different among the types of BBB. The Task force recommend any useful investigation (e.g. CSM, EPS, ILR) to provoke/document the mechanism of syncope before deciding to implant a pacemaker or selecting the correct therapy.
- Elderly patients with bifascicular BBB and unexplained syncope after a reasonable work-up might benefit from empirical pacemaker implantation, especially if syncope is unpredictable (with no- or short prodromes) or has occurred in the supine position or during effort.

Figure 14 Therapeutic algorithm for patients presenting with unexplained syncope and BBB



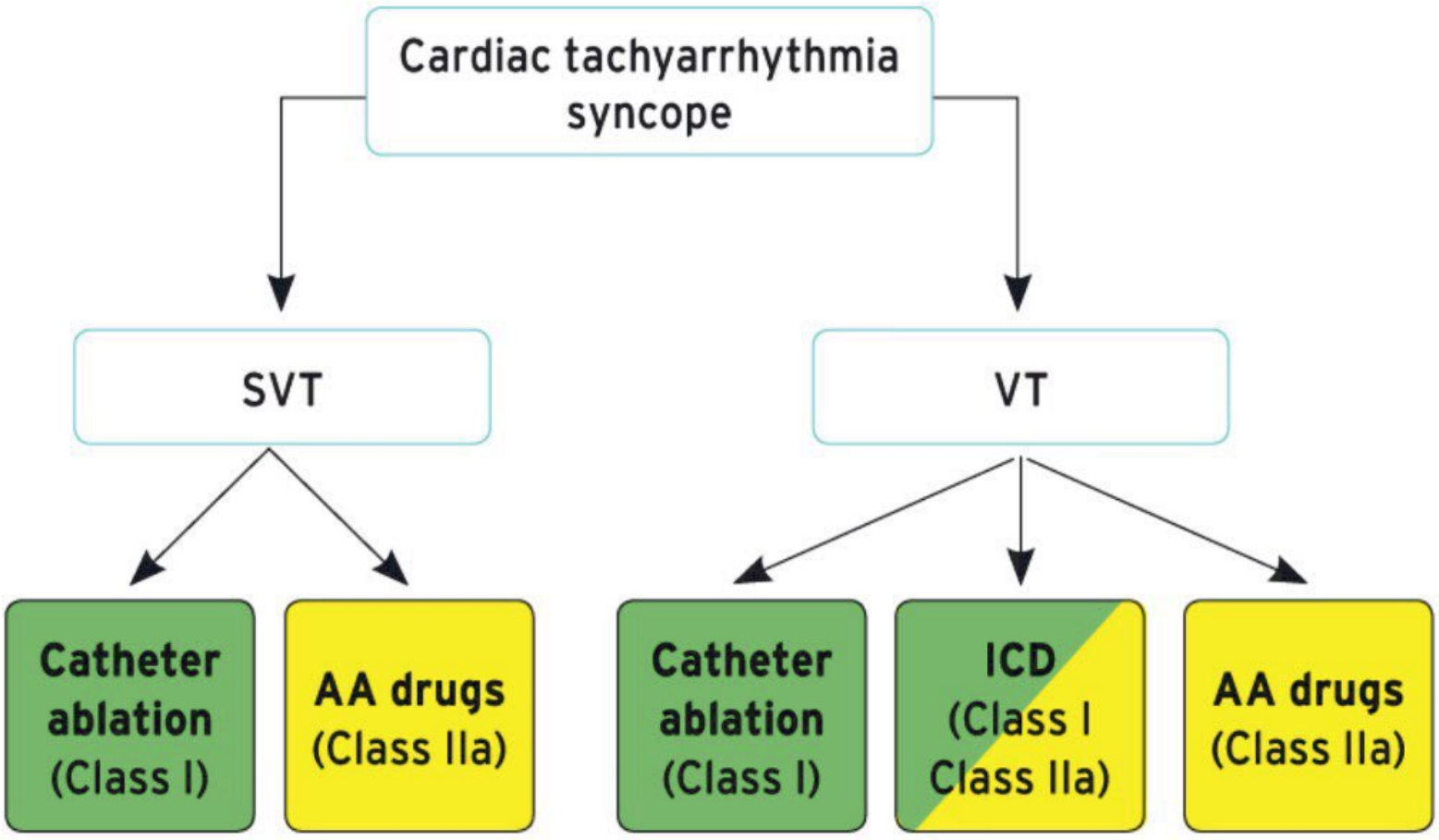
BBB = bundle branch block; CRT-D = cardiac resynchronization therapy defibrillator; EPS = electrophysiological study; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; PM = pacemaker.

For interactivity see here

Treatment of syncope due to intrinsic sinus node dysfunction or atrioventricular conduction system disease		
Recommendations	**Class[a]**	**Level[b]**
Bradycardia (intrinsic)		
Cardiac pacing is indicated when there is an established relationship between syncope and symptomatic bradycardia due to:		
• Sick sinus syndrome	I	B
• Intrinsic AV block	I	B
Cardiac pacing is indicated in patients with intermittent/paroxysmal intrinsic third- or second-degree AV block (including AF with slow ventricular conduction) although there is no documentation of correlation between symptoms and ECG.	I	C
Cardiac pacing should be considered when the relationship between syncope and asymptomatic sinus node dysfunction is less established.	IIa	C
Cardiac pacing is not indicated in patients when there are reversible causes for bradycardia.	III	C
Bifascicular BBB		
Cardiac pacing is indicated in patients with syncope, BBB, and a positive EPS or ILR-documented AV block.	I	B
Cardiac pacing may be considered in patients with unexplained syncope and bifascicular BBB.	IIb	B

AV = atrioventricular; BBB = bundle branch block; ECG = electrocardiogram; EPS =

Figure 15 Choice of therapy for patients presenting with syncope due to cardiac tachyarrhythmias as the primary cause



AA = antiarrhythmic; ICD = implantable cardioverter defibrillator; SVT = supraventricular tachycardia; VT = ventricular tachycardia.

For interactivity see here

When indicated, ICD prevents SCD but it may be unable to prevent syncope due to VT recurrence. Thus, when syncope is due to VT (including when the diagnosis is established by induction of VT during EPS), catheter ablation should be always attempted when feasible in addition to ICD implantation.

Treatment of syncope due to intrinsic cardiac tachyarrhythmias		
Recommendations	**Class[a]**	**Level[b]**
Tachycardia		
Catheter ablation is indicated in patients with syncope due to SVT or VT in order to prevent syncope recurrence.	I	B
An ICD is indicated in patients with syncope due to VT and ejection fraction ≤35%.	I	A
An ICD is indicated in patients with syncope and previous myocardial infarction who have VT induced during EPS.	I	C
An ICD should be considered in patients with ejection fraction >35% with recurrent syncope due to VT when catheter ablation and pharmacological therapy have failed or could not be performed.	IIa	C
Antiarrhythmic drug therapy, including rate-control drugs, should be considered in patients with syncope due to SVT or VT.	IIa	C

EPS = electrophysiological study; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SCD = sudden cardiac death; SVT = supraventricular tachycardia; VT = ventricular tachycardia

[a]Class of recommendation

[b]Level of evidence.

Even in the absence of specific trials, there is strong consensus that with syncope secondary to structural cardiac disease, the goal of treatment is not only to prevent syncopal recurrence, but to treat the underlying disease and decrease the risk of death.

The underlying clinical situation is that of a patient being evaluated for ICD implantation because they are affected by syncope/s supposedly due to transient self-terminating ventricular tachyarrhythmias (fast VT or VF), which had not yet been documented because of its short duration.

Definition

- Unexplained syncope is defined as syncope that does not meet any Class I diagnostic criterion of these guidelines. In the presence of clinical features described in this section, unexplained syncope is considered a suspected arrhythmic syncope.

The presence of syncope increases mortality regardless of its cause. Thus, syncope is a risk factor for life-threatening events.

ICD indications in patients with unexplained syncope and left ventricular systolic dysfunction

Recommendations	Class[a]	Level[b]
ICD therapy is recommended to reduce SCD in patients with symptomatic heart failure (NYHA Class II–III) and LVEF ≤35% after ≥3 months of optimal medical therapy who are expected to survive for at least 1 year with good functional status.	I	A
An ICD should be considered in patients with unexplained syncope with systolic impairment but without a current indication for ICD to reduce the risk of sudden death.	IIa	C
Instead of an ICD, an ILR may be considered in patients with recurrent episodes of unexplained syncope with systolic impairment but without a current indication for ICD.	IIb	C

ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; SCD = sudden cardiac death.

[a]Class of recommendation -[b]Level of evidence.

ICD indications in patients with unexplained syncope and hypertrophy cardiomyopathy

Recommendations	Class[a]	Level[b]
It is recommended that the decision for ICD implantation in patients with unexplained syncope is made according to the ESC HCM Risk- SCD score.[c]	I	B
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope who are at low risk of SCD according to the HCM Risk-SCD score.[c]	IIa	C

ESC = European Society of Cardiology; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SCD = sudden cardiac death.

[a]Class of recommendation -[b]Level of evidence.

[c]A web-based calculator of the HCM risk score can be found in: http://www.-doc2do.com/hcm/webHCM.html

The decision to implant an ICD should take into account the other known risk factors for arrhythmic events: frequent non-sustained VT; family history of premature sudden death; extensive right ventricular disease; marked QRS prolongation; late gadolinium enhancement on magnetic resonance imaging (including left ventricular involvement); left ventricular dysfunction; and VT induction during EPS.

ICD indications in patients with unexplained syncope and arrhythmogenic right ventricular cardiomyopathy

Recommendations	Class[a]	Level[b]
ICD implantation may be considered in patients with ARVC and a history of unexplained syncope.	IIb	C
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope who are at low risk of SCD based on a multiparametric analysis that takes into account the other known risk factors for SCD.	IIa	C

ARVC = arrhythmogenic right ventricular cardiomyopathy; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SCD = sudden cardiac death.

[a]Class of recommendation -[b]Level of evidence.

Beta-blockers are recommended in all patients with a clinical diagnosis of LQTS with the possible exception of those with LQTS-3 form.

ICD indications in patients with unexplained syncope and long QT syndrome

Recommendations	Class[a]	Level[b]
ICD implantation in addition to beta-blockers should be considered in LQTS patients who experience unexplained syncope while receiving an adequate dose of beta-blockers.	IIa	B
Left cardiac sympathetic denervation should be considered in patients with symptomatic LQTS when: (a) beta-blockers are not effective, not tolerated, or are contraindicated; (b) ICD therapy is contraindicated or refused; or (c) when patients on beta-blockers with an ICD experience multiple shocks.	IIa	C
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope who are at low risk of SCD based on a multiparametric analysis that takes into account the other known risk factors for SCD.	IIa	C

ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; LQTS = long QT syndrome; SCD = sudden cardiac death.

[a]Class of recommendation -[b]Level of evidence.

It is reasonable to consider an ICD in the case of unexplained syncope. However, nonarrhythmic syncope is frequent in Brugada syndrome and ICD should be avoided in patients with non-arrhythmic syncope. ILR is increasingly used in doubtful cases to exclude a VA as the cause of syncope. The final decision should also take into account other risk factors for arrhythmic events including spontaneous type I Brugada ECG pattern, family history of sudden death, VF inducibility with 1 or 2 ventricular premature beats during EPS, fractionated QRS, early repolarization in the peripheral leads, increased T_{peak}-T_{end} interval, and long PR interval. A druginduced type 1 ECG pattern has a lower risk of sudden death than a spontaneous type 1 response.

ICD indications in patients with unexplained syncope and Brugada syndrome

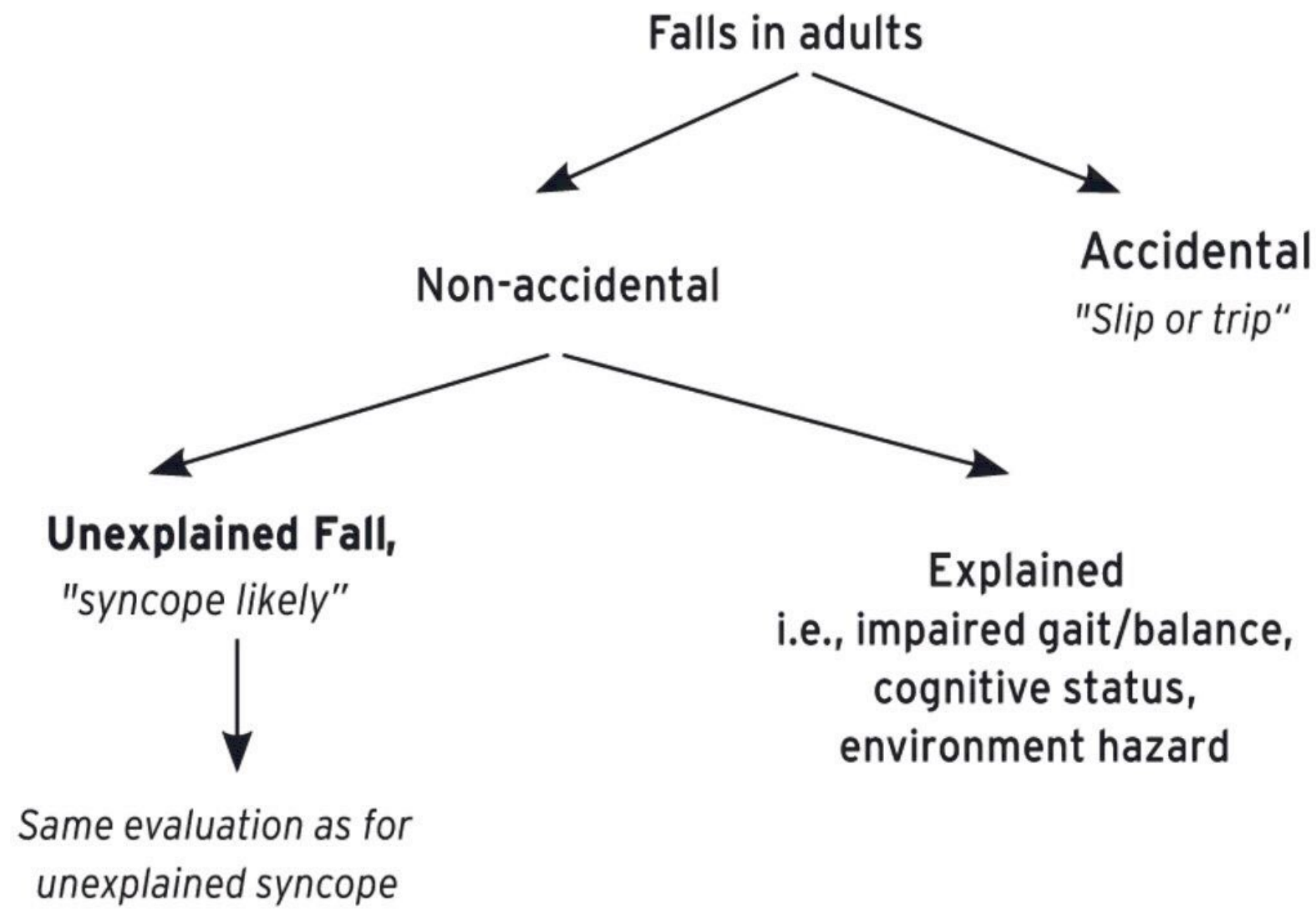
Recommendations	Class[a]	Level[b]
ICD implantation should be considered in patients with a spontaneous diagnostic type 1 ECG pattern and a history of unexplained syncope.	IIa	C
Instead of an ICD, an ILR should be considered in patients with recurrent episodes of unexplained syncope who are at low risk of SCD based on a multiparametric analysis that takes into account the other known risk factors for SCD.	IIa	C

ECG = electrocardiogram; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; SCD = sudden cardiac death.

[a]Class of recommendation -[b]Level of evidence.

- In some frail elderly patients, the rigour of assessment will depend on compliance with tests and on prognosis. Otherwise, evaluation of mobile, non-frail, cognitively normal older adults must be performed as for younger individuals.
- Orthostatic BP measurements, CSM, and tilt testing are well tolerated, even in the frail elderly with cognitive impairment.
- Not infrequently, patients who present with unexplained falls – although orthostatic BP measurements, CSM, and tilt testing reproduce syncope – may deny TLOC, thus demonstrating amnesia for TLOC .
- In the absence of a witness account, the differential diagnosis between falls, epilepsy, TIA, and syncope may be difficult.

Figure 16 Flow diagram for identifying unexplained falls



For interactivity see here

Syncope in patients with comorbidity and frailty		
Recommendations	**Class[a]**	**Level[b]**
A multifactorial evaluation and intervention is recommended in older patients because more than one possible cause for syncope and unexplained fall may be present.	I	B
Cognitive assessment and physical performance tests are indicated in older patients with syncope or unexplained fall.	I	C
Modification or discontinuation of possible culprit medications, particularly hypotensive drugs and psychotropic drugs, should be considered in older patients with syncope or unexplained fall.	IIa	B
In patients with unexplained fall, the same assessment as for unexplained syncope should be considered.	IIa	C

[a]Class of recommendation
[b]Level of evidence.

The diagnosis of PPS rests on positive clues taken from the history and from documenting normal EEG results, HR, or BP during an attack.

Diagnosis and management of psychogenic pseudosyncope

Recommendations	Class[a]	Level[b]
Diagnosis		
Recording of spontaneous attacks with a video by eyewitness should be considered for diagnosis of PPS.	IIa	C
Tilt testing, preferably with concurrent EEG recording and video monitoring may be considered for diagnosis of PPS.	IIb	C
Management		
Doctors who diagnose PPS should present the diagnosis of PPS to the patients.	IIa	C
Cognitive behavioural therapy may be considered in the treatment of PPS if attacks persist after explanation.	IIb	C

EEG = electroencephalogram; PPS = psychogenic pseudosyncope.

[a]Class of recommendation - [b]Level of evidence.

Table 6 Differentiating syncope from epileptic seizures

Clinical feature	Syncope	Epileptic seizures
Useful features		
Presence of trigger	Very often	Rare
Nature of trigger	Differs between types: pain, standing, emotions for VVS; specific trigger for situational syncope; standing for OH	Flashing lights is best known; also range of rare triggers
Prodromes	Often presyncope (autonomic activation in reflex syncope, light-headedness in OH, palpitations in cardiac syncope)	Epileptic aura: repetitive, specific for each patient. Includes déjà vu. Rising sensation in the abdomen (epigastric aura) and/or an unusual unpleasant smell
Detailed characteristics of myoclonus	• <10, irregular in amplitude, asynchronous, asymmetrical • Starts after the onset of LOC	• 20–100, synchronous, symmetrical, hemilateral • The onset mostly coincides with LOC • Clear long-lasting automatisms as chewing or lip smacking at the mouth
Tongue bite	Rare, tip of tongue	Side of tongue (rarely bilateral)
Duration of restoration of consciousness	10–30 seconds	May be many minutes
Confusion after attack	No understanding of situation for <10 seconds in most syncope, full alertness and awareness afterwards	Memory deficit, i.e. repeated questions without imprinting for many minutes
Features of limited utility		
Incontinence	Not uncommon	Common
Presence of myoclonus (see below for nature of myoclonus)	Very often	~60%, dependent on accuracy of observation
Eyes open during LOC	Frequent	Nearly always
Fatigue and sleep afterwards	Common, particularly in children	Very common
Blue face	Rare	Fairly often

LOC = loss of consciousness; OH = orthostatic hypotension; VVS = vasovagal syncope.

Epilepsy may trigger syncope ("ictal asystole"). Epileptic asystole occurs during partial complex seizures. A typical history is for a partial complex seizure followed by asystole due to vagal activation brought about by the seizure. Therapy requires antiepileptic drugs and possibly a pacemaker.

In general, a TIA concerns a focal neurological deficit without LOC, and syncope the opposite. A TIA related to a carotid artery does not usually cause TLOC. A TIA of the vertebrobasilar system can cause LOC, but there are always focal signs.

Syncope, presumable VVS, and orthostatic intolerance occur more often in patients with migraine, who have a higher lifetime prevalence of syncope and often frequent syncope.

Cataplexy concerns paresis or paralysis triggered by emotions, usually laughter. Cataplexy is a key feature of narcolepsy; other cardinal symptoms are excessive daytime sleepiness, sleep onset paralysis, and hypnagogic hallucinations.

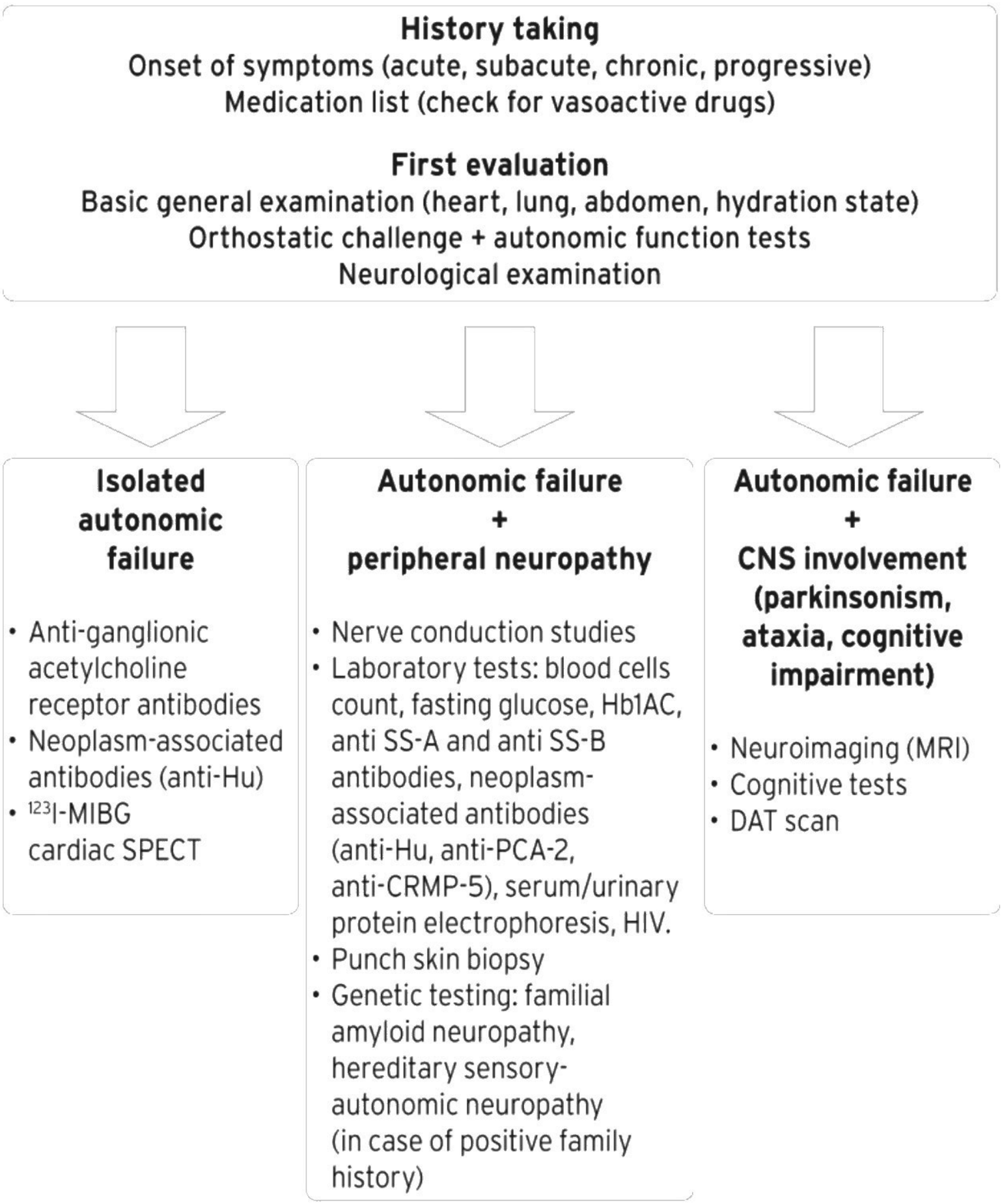
The term drop attacks is confusing. A specific condition also labelled drop attacks concerns middle-aged women (rarely men) who suddenly find themselves falling. They usually remember hitting the floor and can stand up immediately afterwards.

Neurological evaluation

Recommendations	Class[a]	Level[b]
Neurological evaluation is indicated when syncope is due to autonomic failure to evaluate the underlying disease.	I	C
Neurological evaluation is indicated in patients in whom TLOC is suspected to be epilepsy.	I	C

TLOC = transient loss of consciousness.
[a]Class of recommendation - [b]Level of evidence.

Figure 17 Diagnostic work-up of cardiovascular autonomic failure



^{123}I-MIBG = ^{123}I-metaiodobenzylguanidine; CNS = central nervous system; CRMP-5 = collapsin response mediator protein 5; DAT = dopamine active transporter; HbA1c = haemoglobin A1c; HIV = human immunodeficiency virus; MRI = magnetic resonance imaging; PCA-2 = Purkinje cell cytoplasmic autoantibody type 2; SPECT = single-photon emission computed tomography; SS-A = Sjogren's syndrome-associated antigen A; SS-B = Sjogren's syndrome-associated antigen B.

Neurological tests

Recommendations	Class[a]	Level[b]
Brain magnetic resonance imaging is recommended if neurological examination indicates Parkinsonism, ataxia, or cognitive impairment.	I	C
Screening for paraneoplastic antibodies and antiganglionic acetylcholine receptor antibodies is recommended in cases of acute or subacute onset of multidomain autonomic failure.	I	C
EEG, ultrasound of neck arteries, and computed tomography or magnetic resonance imaging of the brain are not indicated in patients with syncope.	III	B

EEG = electroencephalogram.
[a]Class of recommendation - [b]Level of evidence.

Definition of a syncope unit

A syncope unit is a facility featuring a standardized approach to the diagnosis and management of TLOC and related symptoms, with dedicated staff and access to appropriate diagnostics and therapies.

The syncope specialist is defined as one who has responsibility for the comprehensive management of the patient from risk stratification to diagnosis, therapy, and followup, through a standardized protocol. A syncope specialist is a physician who has sufficient knowledge of historical clues and physical findings to recognize all major forms of TLOC, including mimics, as well as syndromes of orthostatic intolerance.

Although the benefit of a syncope unit or a syncope specialist in the different healthcare systems has not been exposed to rigorous scientific or economic scrutiny, the consensus is that a dedicated service (a syncope unit) affords better management of TLOC, from risk stratification to diagnosis, therapy, and follow-up, and better education and training of stakeholders. Further research is likely to have an important impact on our confidence in the estimate of effect.

Table 7 Key components of a syncope unit

- The syncope unit should take the lead in service delivery for syncope, and in education and training of healthcare professionals who encounter syncope.
- The syncope unit should be led by a clinician with specific knowledge of TLOC and additional necessary team members (i.e. clinical nurse specialist) depending on the local model of service delivery.
- The syncope unit should provide minimum core treatments for reflex syncope and OH, and treatments or preferential access for cardiac syncope, falls, psychogenic pseudosyncope, and epilepsy.
- Referrals should be directly from family practitioners, EDs, in-hospital and outhospital services, or self-referral depending on the risk stratification of referrals. Fast-track access, with a separate waiting list and scheduled follow-up visits, should be recommended.
- Syncope units should employ quality indicators, process indicators, and desirable outcome targets.

Structure of the syncope unit

Table 8 Structure of the syncope unit

Staffing of a syncope unit is composed of:

1. One or more physicians of any specialty who are syncope specialists. Owing to the multidisciplinary nature of TLOC management, each syncope unit should identify specific specialists for the syncope unit and for consultancies.
2. A staff comprising professionals who will advance the care of patients with syncope. These may be physicians, specialized nurses, or others who bring multidisciplinary skills to the facility, coupled with administrative support. The roles played by members of the team may vary according to local circumstances and individual skill. Nurses may be expected to take very important roles including initial assessment, follow-up clinic evaluation, selection of investigations (including tilt testing), and implantation/insertion of ECG loop recorders according to predefined protocols and local regulations.
3. Given that the syncope unit is integrated within a hospital organization, syncope specialists and staff are not necessarily employed full-time, but frequently have other duties depending on the volume of activity in the unit.

Facility, protocol, and equipment

1. A syncope unit will deliver most of its care to outpatients in addition to ED and inpatients.
2. The syncope unit should follow an internal protocol, which applies to diagnosis and management and is agreed by stakeholders.
3. An equipped facility must be available.
4. Essential equipment/tests:
   - 12-lead ECG and 3-lead ECG monitoring.
   - Non-invasive beat-to-beat BP monitor with recording facilities for subsequent analysis
   - Tilt-table.
   - Holter monitors/external loop recorders.
   - ILRs
   - Follow-up of ILRs[a]
   - 24-hour BP monitoring.
   - Basic autonomic function tests.
5. Established procedures for:
   - Echocardiography
   - EPS
   - Stress test
   - Neuroimaging tests.
6. Specialists' consultancies (cardiology, neurology, internal medicine, geriatric, psychology), when needed.

Therapy

Patients with syncope will receive their therapy under the care of the syncope unit unless expertise outside that of the unit is required.

Database management

The syncope unit is required to keep medical records that should also include follow-up when appropriate. The database will also offer the possibility of collaborative research with other syncope units.

BP = blood pressure; ECG = electrocardiogram; ED = emergency department; EPS = electrophysiological study; ILR = implantable loop recorder; TLOC = transient loss of consciousness.

[a]Implantation of loop recorders may be performed either by syncope unit physicians or by external cardiologists upon request of the syncope unit physicians.

Table 9 Test and assessments available in a syncope unit

Initial assessment	
History and physical evaluation including 3-min orthostatic BP measurementa 12-lead standard ECG	
Subsequent tests and assessments (only when indicated)	
Blood tests	Electrolytes, haemoglobin, troponin, B-type natriuretic peptide, glucose, D-dimer, haemogas analysis/oxygen saturation
Provocative tests	CSM, tilt testing
Monitoring	External loop recording, implantable loop recording, ambulatory 1–7 days ECG monitoring, 24–48-hour BP monitoring
Autonomic function tests	Standing test, Valsalva manoeuvre, deep-breathing test, cold pressor test, and/or established procedures for access to other autonomic function tests
Cardiac evaluation	Established procedures for access to echocardiogram, stress test, electrophysiological study, coronary angiography
Neurological evaluation	Established procedures for access to neurological tests (computed tomography, magnetic resonance imaging, EEG, video-EEG)
Geriatric evaluation	Established procedures for access to fall risk assessment (cognitive, gait and balance, visual, environmental) and for gait and balance retraining
Psychological or psychiatric evaluation	Established procedures for access to psychological or psychiatric consultancy (mental health problem or psychogenic syncope)

BP = blood pressure; CSM = carotid sinus massage; ECG = electrocardiogram; EEG = electroencephalogram; min = minutes. [a]Postural orthostatic tachycardia may require longer period of standing.

Table 10 The role of physician and staff in performing procedures and tests

Procedure or test	Syncope unit physician	Syncope unit staff	Nonsyncope unit personnel
History taking	X		
Structured history taking (e.g. application of software technologies and algorithms)		X	
12-lead ECG		X	
Blood tests		X	
Echocardiogram and imaging			X
CSM	X		
Active standing test		X	
Tilt testing	(X)[a]	X	
Basic autonomic function test		X	
ECG monitoring (Holter, external loop recorder): administration and interpretation	X	X	
ILR	X	(X)[b]	
Remote monitoring		X	
Other cardiac tests (stress test, EPS, angiograms)			X
Neurological tests (computed tomography, magnetic resonance imaging, EEG, video-EEG)			X
Pacemaker and ICD implantation, catheter ablation			X
Patient education, biofeedback trainingc and instruction sheet on PCM	X	X	
Final report and clinic note	X		
Communication with patients, referring physicians, and stakeholders.	X	X	
Follow-up	X	X	

BP = blood pressure; CSM = carotid sinus massage; ECG = electrocardiogram; EEG = electroencephalogram; EPS = electrophysiological study; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; PCM = physical counter-pressure manoeuvres. [a]Physician need not be in the room, but a physician adequately trained in resuscitation needs to be in the vicinity of the test - [b]Current practice limited to a few countries - [c]Biofeedback means that the PCM training session consists of biofeedback training using a continuous BP monitor. Each manoeuvre is demonstrated and explained. The manoeuvres are practised under supervision, with immediate feedback of the recordings to gain optimal performance.